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Jan DELAVAL

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# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Josephine Young Examiner #: 77813 Date: 12/12/02  
 Art Unit: 1123 Phone Number 301-605-1201 Serial Number: 091587,662  
 Mail Box and Bldg/Room Location: CM1 8D04 Results Format Preferred (circle): PAPER DISK (E-MAIL)

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*  
 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods and Compositions for Modulating Drug Activity through Targeted  
 Inventors (please provide full names): AU, Jesse L.S.;  
WENTJES, M. Guillaume

Earliest Priority Filing Date: 06/04/1999

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Attached: 1) Bib Sheet; ~~2) Abstract~~; 3) Pending Claims (1-28; 33-35; 40-48)  
Case Assigned to me

Please search: 1) ~~methods to treat cancer/abuse cell pol(1-1)~~  
w/ antisense drug agent AND  
b) antisense inhibitory agent

2) ~~methods to treat cancer/abuse cell pol(1-1)~~  
w/ pectin + b) antisense nucleic acid sequence, AZT, etc  
(or other nucleoside/nucleotide analogs) - e.g. d, l, etc  
comb. with pectin and AZT, etc  
dit

See claims 1, 23-27, 40, 42, 44-48

Thanks!

Jan Delaval  
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 Biotechnology & Chemical Library  
 CM1 1E07 - 703-308-4498  
 jan.delaval@uspto.gov

03-1215102 - 92-170

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| Date Searcher Picked Up: <u>12/15/02</u> | Bibliographic <u>✓</u> | Dr. Link _____                    |
| Date Completed: <u>12/15/02</u>          | Litigation _____       | Lexis/Nexis _____                 |
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| Clerical Prep Time: <u>15</u>            | Patent Family _____    | WWW/Internet _____                |
| Online Time: <u>5:20</u>                 | Other _____            | Other (specify) _____             |

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STRUCTURE FILE UPDATES: 13 DEC 2002 HIGHEST RN 476274-11-0  
DICTIONARY FILE UPDATES: 13 DEC 2002 HIGHEST RN 476274-11-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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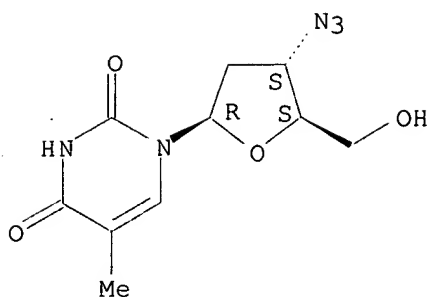
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d ide can tot 15

L5 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS  
RN 30516-87-1 REGISTRY  
CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 3'-Azido-3'-deoxythymidine  
CN 3'-Azidothymidine  
CN 3'-Deoxy-3'-azidothymidine  
CN 874: PN: WO02055741 SEQID: 889 claimed sequence  
CN Azidothymidine  
CN Azitidin  
CN AZT  
CN AZT (pharmaceutical)  
CN BW-A 509U  
CN NSC 602670  
CN Retrovir  
CN Retrovir IV  
CN Timazid  
CN ZDV  
CN Zidovudine  
FS STEREOSEARCH  
DR 399024-19-2  
MF C10 H13 N5 O4  
CI COM  
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,  
'CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES,  
DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB\*, IFICDB, IFIPAT,  
IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH,  
PIRA, PROMT, RTECS\*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN,  
USPAT2, USPATFULL, VETU  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, WHO  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+)...



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4190 REFERENCES IN FILE CA (1962 TO DATE)  
 166 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 4208 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:370337  
 REFERENCE 2: 137:369566  
 REFERENCE 3: 137:365526  
 REFERENCE 4: 137:364613  
 REFERENCE 5: 137:363028  
 REFERENCE 6: 137:358121  
 REFERENCE 7: 137:346131  
 REFERENCE 8: 137:345638  
 REFERENCE 9: 137:345635  
 REFERENCE 10: 137:345623

L5 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS  
 RN 3056-17-5 REGISTRY  
 CN Thymidine, 2',3'-didehydro-3'-deoxy- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 2'-Thymidinene, 3'-deoxy- (8CI)  
 CN Thymine, 1-(2,3-dideoxy-.beta.-D-glycero-pent-2-enofuranosyl)- (7CI, 8CI)  
 OTHER NAMES:  
 CN 2',3'-Didehydro-3'-deoxythymidine  
 CN 3'-Deoxy-2',3'-didehydrothymidine  
 CN 879: PN: WO02055741 SEQID: 894 claimed sequence  
 CN BMY 27857  
 CN D 4T  
 CN D 4T (nucleoside)  
 CN Sanilvudine  
 CN Stavudine  
 CN Zerit  
 FS STEREOSEARCH  
 DR 132425-31-1  
 MF C10 H12 N2 O4  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*,

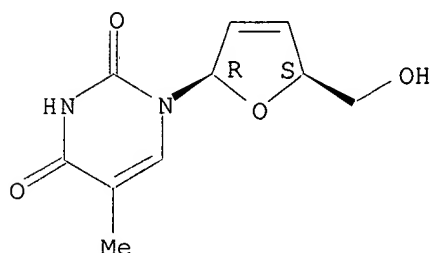


BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK\*, PHAR, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1177 REFERENCES IN FILE CA (1962 TO DATE)  
 30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 1186 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363028  
 REFERENCE 2: 137:346131  
 REFERENCE 3: 137:345638  
 REFERENCE 4: 137:345635  
 REFERENCE 5: 137:342084  
 REFERENCE 6: 137:333119  
 REFERENCE 7: 137:332775  
 REFERENCE 8: 137:320060  
 REFERENCE 9: 137:319998  
 REFERENCE 10: 137:310928

=> d ide can 13

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 33069-62-4 REGISTRY

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

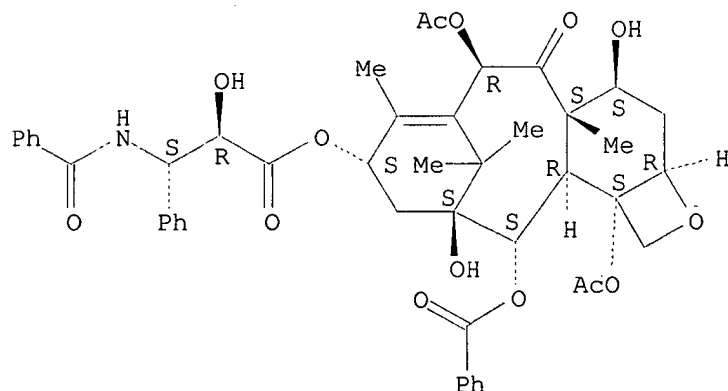
CN 7,11-Methano-1H-cyclodeca[3,4]benz[1,2-b]oxete, benzenepropanoic acid  
 deriv.

- CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R\*,.beta.S\*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-
- CN Tax-11-en-9-one, 5.beta.,20-epoxy-1,2.alpha.,4,7.beta.,10.beta.,13.alpha.-hexahydroxy-, 4,10-diacetate 2-benzoate 13-ester with (2R,3S)-N-benzoyl-3-phenylisoserine (8CI)

## OTHER NAMES:

- CN ABI 007
- CN BMS 181339-01
- CN NSC 125973
- CN **Paclitaxel**
- CN Plaxicel
- CN Taxol
- CN Taxol A
- CN Yewtaxan
- FS STEREOSEARCH
- MF C47 H51 N O14
- CI COM
- LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM\*, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB\*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU (\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



6638 REFERENCES IN FILE CA (1962 TO DATE)  
 360 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 6666 REFERENCES IN FILE CAPLUS (1962 TO DATE)

- REFERENCE 1: 137:375308
- REFERENCE 2: 137:375278
- REFERENCE 3: 137:375259
- REFERENCE 4: 137:375077
- REFERENCE 5: 137:371619
- REFERENCE 6: 137:370237

REFERENCE 7: 137:369971  
REFERENCE 8: 137:369559  
REFERENCE 9: 137:368586  
REFERENCE 10: 137:365210

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L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
RN 120178-12-3 REGISTRY  
CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA  
INDEX NAME)  
OTHER NAMES:  
CN DNA telomerase  
CN Subunit (Mesocricetus auratus)  
CN **Telomerase**  
CN Telomerase reverse transcriptase  
MF Unspecified  
CI MAN  
SR CA  
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS,  
CBNB, CEN, CIN, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
2901 REFERENCES IN FILE CA (1962 TO DATE)  
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
2911 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:375238  
REFERENCE 2: 137:367532  
REFERENCE 3: 137:367487  
REFERENCE 4: 137:367406  
REFERENCE 5: 137:367380  
REFERENCE 6: 137:365746  
REFERENCE 7: 137:364456  
REFERENCE 8: 137:364455  
REFERENCE 9: 137:364356  
REFERENCE 10: 137:364304

=> d his

(FILE 'HOME' ENTERED AT 11:30:34 ON 15 DEC 2002)  
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FILE 'REGISTRY' ENTERED AT 11:30:44 ON 15 DEC 2002

E AZT/CN  
L1 1 S E4  
E D4T/CN  
E D 4T/CN  
L2 1 S E4

L3           E PACLITAXEL/CN  
           1 S E3  
           E TELOMERASE/CN  
 L4           1 S E3  
 L5           2 S L1,L2  
           SEL RN  
 L6           57 S E1-E2/CRN  
           SEL RN L3  
 L7           44 S E3/CRN  
 L8           0 S L6 AND L7  
 L9           11 S L6 NOT MXS/CI  
 L10          7 S L9 NOT COMPD  
 L11          22 S L7 NOT CYCLODEXTRIN  
 L12          16 S L11 NOT COMPD  
 L13          5 S L12 AND (CLH OR H2O OR C2H4O)  
 L14          4 S L13 NOT IDS/CI  
 L15          22 S L7 NOT L11  
 L16          27 S L3,L14,L15  
 L17          9 S L5,L10

FILE 'HCAPLUS' ENTERED AT 11:37:30 ON 15 DEC 2002

L18          4612 S L17  
 L19          5162 S AZT OR ZIDOVUDIN# OR AZITIDIN# OR AZIDOTHYIMIDIN# OR RETROVIR#  
 L20          1316 S D4T OR D 4T OR STAVUDIN# OR SANILVUDIN# OR ZERIT OR BMY27857  
 L21          6072 S L18-L20  
 L22          6664 S L16  
 L23          9158 S PACLITAXEL OR TAXOL  
 L24          9195 S L22,L23  
 L25          58 S L21 AND L24  
 L26          2912 S L4  
 L27          3658 S TELOMERASE  
 L28          3661 S L26,L27  
 L29          2 S L25 AND L28  
           E AU J/AU  
 L30          104 S E3,E6-E9,E15-E18  
           E WIENTJES G/AU  
 L31          8 S E4-E7  
 L32          3 S L30,L31 AND L28  
 L33          1 S L30,L31 AND L25  
 L34          4 S L29,L32,L33  
           E WIENTJES M/AU  
 L35          69 S E3-E7  
 L36          2 S L35 AND L28  
 L37          0 S L35 AND L25  
 L38          4 S L34,L36  
 L39          2 S L25 AND ?TELOMER?  
 L40          4 S L38,L39  
           E ANTISENSE/CT  
           E E4+ALL  
 L41          3417 S E6,E5  
           E E7+ALL  
 L42          6709 S E9  
           E E14+ALL  
 L43          3303 S E6,E7,E5  
           E NUCLEOTIDES/CT  
           E E3+ALL  
 L44          253674 S E7+NT  
 L45          367 S L24 AND L41-L44  
 L46          4 S L45 AND L28  
 L47          22 S L24 AND ?TELOMER?  
 L48          24 S L40,L46,L47

FILE 'REGISTRY' ENTERED AT 11:53:10 ON 15 DEC 2002

L49 1 S 120178-12-3  
L50 1 S L49,L4

FILE 'HCAPLUS' ENTERED AT 11:53:23 ON 15 DEC 2002

L51 17 S L50 AND L48  
L52 20 S L48,L51 AND (1 OR 63)/SC,SX  
L53 4 S L48 NOT L52  
L54 22 S L40,L52  
L55 8 S L54 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L56 11 S L40,L55  
L57 56 S L25 NOT L48,L56  
L58 41 S L57 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L59 41 S L58 AND L18  
L60 41 S L59 AND L22  
L61 32 S L60 AND (?NEOPLAS? OR ?TUMOR? OR ?MALIGNAN? OR ?CANCER? OR ?C  
L62 27 S L60 AND (MIX? OR SYNERG? OR COMPOSITION OR COTHERAP? OR COMED  
L63 23 S L61 AND L62  
SEL DN AN 8 9 10 13 14 15 19  
L64 7 S E1-E21  
L65 18 S L56,L64 AND L18-L48,L51-L64

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FILE LAST UPDATED: 13 Dec 2002 (20021213/ED)

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=> d l65 all hitstr tot

L65 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2002 ACS  
AN 2002:684654 HCAPLUS  
TI Telomere maintenance in **telomerase**-positive human ovarian SKOV-3 cells cannot be retarded by complete inhibition of **telomerase**  
AU Gan, Yuebo; Mo, Yiqun; Johnston, Jeffrey; Lu, Jie; Wientjes, M. Guillaume; Au, Jessie L.-S.  
CS College of Pharmacy, The Ohio State University, Columbus, OH, 43210, USA  
SO FEBS Letters (2002), 527(1-3), 10-14  
CODEN: FEBLAL; ISSN: 0014-5793

PB Elsevier Science B.V.

DT Journal

LA English

CC 13 (Mammalian Biochemistry)

AB The two known mechanisms for telomere maintenance in eukaryocytes are **telomerase** in **telomerase-pos.** cells and alternative lengthening of telomeres (ALT) in **telomerase-neg.** cells. We report here that telomere maintenance in the **telomerase-pos.** human ovarian SKOV-3 cells was not affected by inhibition of **telomerase**. For comparison, the effect of **telomerase** inhibitors on telomere maintenance in another **telomerase-pos.** cell line (i.e. human pharynx FaDu cells) and the **telomerase-neg.** human osteosarcoma Saos-2 cells was examd. **Telomerase** activity was measured using a modified telomeric repeat amplification protocol and telomere length was measured using a soln. hybridization-based method and fluorescence in situ hybridization. A reverse transcriptase inhibitor (3'-azido-deoxythymidine or **AZT**) and an antisense against a component of human **telomerase** RNA (antisense hTR) were used to inhibit **telomerase**. FaDu and SKOV-3 cells showed comparable baseline **telomerase** activity. **Telomerase** activity in both cells was inhibited about equally by **AZT** (maximal inhibition of .apprx.80%) and by expression of antisense hTR (complete inhibition in SKOV-3 cells and maximal inhibition of .apprx.80% in FaDu cells). However, treatment with **telomerase** inhibitors resulted in .apprx.50% telomere shortening in FaDu cells but had no effect on SKOV-3 nor Saos-2 cells. SKOV-3 cells did not show the characteristic features of ALT (i.e. heterogeneous telomere length and promyelocytic leukemia bodies), whereas these ALT features were obsd. in Saos-2 cells. Collectively, these results suggest the existence of a **telomerase-independent** mechanism of telomere maintenance in the **telomerase-pos.** SKOV-3 cells.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Biessmann, H; Chromosoma 1997, V106, P63 HCAPLUS
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- (28) Zakian, V; Science 1995, V270, P1601 HCAPLUS

AN 2002:521462 HCAPLUS  
 DN 137:88442  
 TI Incensole and furanogermacrems and compounds in treatment for inhibiting  
 neoplastic lesions and microorganisms  
 IN Shanahan-Pendergast, Elisabeth  
 PA Ire.  
 SO PCT Int. Appl., 68 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC A61K031-00  
 CC 1-6 (Pharmacology)  
 Section cross-reference(s): 10, 63

FAN.CNT 1

|      | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|------|--|------|----------|-----------------|----------|
| PI   | WO 2002053138  | A2   | 20020711 | WO 2002-IE1     | 20020102 |
|      | WO 2002053138  | A3   | 20020919 |                 |          |
|      | W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM  |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG   |      |          |                 |          |
| PRAI | IE 2001-2  | A    | 20010102 |                 |          |
| OS   | MARPAT 137:88442   |      |          |                 |          |
| AB   | The invention discloses the use of incensole and/or furanogermacrems, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixt. showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis. |      |          |                 |          |
| ST   | neoplastic lesion treatment incensole furanogermacren compd; antitumor incensole furanogermacren; antimicrobial incensole furanogermacren  |      |          |                 |          |
| IT   | Proteins<br>RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)<br>(A, immunomodulator based on, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)   |      |          |                 |          |
| IT   | Leukemia<br>Lymphoma<br>(B-cell; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)   |      |          |                 |          |
| IT   | Intestine, disease<br>(Crohn's, treatment of; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)  |      |          |                 |          |
| IT   | Canarypox virus<br>(IL-2 of, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)   |      |          |                 |          |
| IT   | GTPase-activating protein<br>RL: BSU (Biological study, unclassified); BIOL (Biological study)<br>(Ras-GAP, inhibitors, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)  |      |          |                 |          |
| IT   | Proteins<br>RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)<br>(Sdi 1, mimetics, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)   |      |          |                 |          |
| IT   | Skin, neoplasm<br>(Sezary syndrome; incensole and furanogermacrems and compds. as  |      |          |                 |          |

- antitumor and antimicrobial agents)
- IT Leukemia
  - Lymphoma
    - (T-cell; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Transcription factors
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (WT1 (Wilms' tumor suppressor 1), therapy based on; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Keratosis
  - (actinic; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Leukemia
  - (acute; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Lung, neoplasm
  - (adenocarcinoma; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Melanoma
  - (amelanotic; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Urokinase-type plasminogen activator receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (antagonists, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Nutrients
  - (anti-, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Proteins
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (anti-dorsalizing morphogenetic protein-1, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Androgens
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (antiandrogens, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Estrogens
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (antiestrogens, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Antitumor agents
  - (antineoplastons, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Drug resistance
  - (antitumor; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Lung, disease
  - (aspergillosis, treatment of immunodysregulation condition caused by; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Infection
  - (bacterial, intracellular or extracellular, treatment of immunodysregulation condition caused by; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Candida
  - (candidiasis from, treatment of immunodysregulation condition caused by; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)



- antimicrobial agents)
- IT Prostate gland
  - (carcinoma, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Ovary, neoplasm
- Stomach, neoplasm
  - (carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Mycobacterium
  - (cell wall sk and monophosphoryl lipid A, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Diterpenes
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (cembranoid, alcs.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Diterpenes
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (cembranoid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Nervous system
  - (central, disease, precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Nervous system
  - (central, neoplasm; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Uterus, disease
  - (cervix, dysplasia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Uterus, neoplasm
  - (cervix; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Porphyrins
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (chlorins, benzo-, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Porphyrins
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (chlorins, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Leukemia
  - (chronic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Polymers, biological studies
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (co-, enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Intestine, neoplasm
  - (colon, carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Intestine, neoplasm
  - (colon, polyp; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Intestine
  - (colon, precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Intestine, neoplasm
  - (colon; incensole and furanogermacrens and compds. as antitumor and

- antimicrobial agents)
- IT Polyoxyalkylenes, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(conjugates with pyridoxylated Hb; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Quinones  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclopentantraquinones, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Bronchi  
Prostate gland  
(disease, dysplasia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Mammary gland  
(disease, precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Bladder  
(diseases, lesions; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Immunity  
(disorder, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Carbohydrates, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drug delivery systems contg.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Antibodies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drug targeting to HIV infected cells using; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Skin, neoplasm  
(dysplastic nevus syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Dendritic cell  
(enhancement of endogenous precursor; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Heat-shock proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(enhancement of endogenous; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Polymers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(enteric-coated; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(enteric; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Escherichia coli  
(enterohemorrhagic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Escherichia coli  
(enteroinvasive, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Escherichia coli  
(enteropathogenic, treatment of immunodysregulation condition caused by

- infection with; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Escherichia coli  
(enterotoxigenic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Lung, neoplasm  
(epidermoid; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Gene therapy  
(erythrocyte, vector system, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Gene, animal  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(for apoptosis, modulators of, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Fusion proteins (chimeric proteins)  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gene BCR-ABL, antagonists, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gene c-raf, antagonists, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Multidrug resistance  
(gene inhibitor, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Apoptosis  
(gene modulators or regulators, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Erythrocyte  
(gene therapy vector system, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Envelope proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gp120env, drug targeting to HIV infected cells using antibodies to; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Envelope proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gp160env, drug targeting to HIV infected cells using antibodies to; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Leukemia  
(hairy-cell; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(immunostimulant, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Chemotherapy  
Parasitocides  
Radiotherapy  
Surgery

- (in combination with; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Adrenal gland, neoplasm  
Anti-AIDS agents  
Anti-infective agents  
Antiarthritics  
Antiasthmatics  
Antidiabetic agents  
Antidiarrheals  
Antitumor agents  
Brain, neoplasm  
Burn  
Drug delivery systems  
Drug targeting  
Enterococcus faecalis  
Hodgkin's disease  
Human  
Lymphoma  
Mammalia  
Melanoma  
Multiple myeloma  
Neoplasm  
Newborn  
Ovary, neoplasm  
Pancreas, neoplasm  
Sarcoma  
Staphylococcus aureus  
Stomach, neoplasm  
Testis, neoplasm  
(incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Yeast  
(infection with, treatment of immunodysregulation condition caused by; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Intestine, disease  
(inflammatory, treatment of; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Cartilage  
(inhibitor derived from, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Insulin-like growth factor I receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Translation, genetic  
(inhibitors of, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Signal transduction, biological  
(inhibitors or modulators, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Macrophage migration inhibitory factor  
Ras proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT Insulin-like growth factor-binding proteins  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(insulin-like growth factor I-binding, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as

- antitumor and antimicrobial agents)
- IT Parasite  
(intracellular or extracellular infection with, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Gamma ray  
(irradn., treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Intestine, disease  
(irritable bowel syndrome, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Digestive tract  
(irritation, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Paracoccidioides  
(juvenile paracoccidiomyosis, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Lung, neoplasm  
(large-cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Skin, disease  
(lesions; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Virus  
(lipid envelope, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(lipophilic disaccharide, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(liposomes; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(lytic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Pulverization  
(micronization; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Double stranded RNA  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mismatched, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Antibodies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal, conjugates, with liposome or carbohydrate vehicles, to tumor-assocd. antigen; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Antibodies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal, to human chorionic gonadotropin, pharmaceutical formulation further including; incensole and furanogermacrens and

- compsds. as antitumor and antimicrobial agents)
- IT Leukemia  
(monocytic; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Lipid A  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monophosphates, and mycobacterium cell wall sk, pharmaceutical formulation further including; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Nerve, disease  
(motor, treatment of; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Gram-positive bacteria (Firmicutes)  
(multi-drug resistant; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Gene  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(multidrug resistance, inhibitor, pharmaceutical formulation further including; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Leukemia  
(myelogenous; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Leukemia  
(myelomonocytic; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(nasal; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Bladder  
Mammary gland  
Mouth  
Prostate gland  
(neoplasm; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Nerve, neoplasm  
(neuroblastoma; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Antioxidants  
(nitroxide, pharmaceutical formulation further including; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Lymphocyte  
(null cell, leukemia; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Interleukin 2  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(of canarypox virus, pharmaceutical formulation further including; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Cytokines  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(oral inducer, pharmaceutical formulation further including; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(oral; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(parenterals; incensole and furanogermacrems and compsds. as antitumor and antimicrobial agents)
- IT Antiviral agents  
(pharmaceutical formulation further contg.; incensole and

- furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Interferons
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (pharmaceutical formulation further contg.; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Angiogenesis inhibitors
  - Antivenoms
  - Cytotoxic agents
  - Immunostimulants
  - Mycobacterium bovis
  - Venoms
  - (pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT **Antisense oligonucleotides**
  - Estrogens
  - Heregulins
  - Hormones, animal, biological studies
  - Interleukins
  - Leukemia inhibitory factor
  - Oligonucleotides**
  - Polyamines
  - Ribozymes
  - Steroids, biological studies
  - Taxanes
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Disease, animal
  - (polyposis syndrome; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Fatty acids, biological studies
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (poppy seed-oil, Et esters, labeled with iodine-131, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Kidney, disease
  - Lung, disease
  - Stomach, disease
  - (precancerous lesion in; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Drug delivery systems
  - (prodrugs; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Hemoglobins
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (reaction products, with pyridoxal phosphate, conjugates with polyoxyethylene, pharmaceutical formulation further including; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Drug delivery systems
  - (rectal; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Kidney, neoplasm
  - (renal cell carcinoma; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Antitumor agents
  - (resistance to; incensole and furanogermacrems and compds. as antitumor and antimicrobial agents)
- IT Proteins

- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(saporins, fibroblast growth factor conjugates; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Proteins  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(senescence-derived inhibitor 1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT **Oligonucleotides**  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sense, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Shock (circulatory collapse)  
(septic, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Proteins  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(single chain antigen binding protein, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Cell wall  
(sk of mycobacteria and monophosphoryl lipid A, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Leukemia  
(small cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Lung, neoplasm  
(small-cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Neoplasm  
(solid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Carcinoma  
(squamous cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Cell  
(stem, division inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Cell  
(stem, inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Drug delivery systems  
(sublingual; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Glycosaminoglycans, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(synthetic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Lupus erythematosus  
(systemic, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Human immunodeficiency virus  
(targeting to cells infected with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
- IT Receptors



RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(thymopoietin, agonists, pharmaceutical formulation further including;  
incensole and furanogermacrene and compounds. as antitumor and  
antimicrobial agents)

IT Drug delivery systems  
(topical; incensole and furanogermacrene and compounds. as antitumor and  
antimicrobial agents)

IT Stem cell factor  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(totipotent, pharmaceutical formulation further including; incensole  
and furanogermacrene and compounds. as antitumor and antimicrobial agents)

IT Adeno-associated virus  
Balantidium  
Balantidium coli  
Borrelia  
Campylobacter  
Candida  
Coronavirus  
Cryptococcus (fungus)  
Cryptosporidium  
DNA viruses  
Entamoeba  
Entamoeba histolytica  
Filovirus  
Flavivirus  
Haemophilus  
Hantavirus  
Human papillomavirus  
Human parainfluenza virus  
Human poliovirus  
Influenza virus  
Legionella  
Leishmania  
Leishmania braziliensis  
Leishmania donovani  
Leishmania mexicana  
Leishmania tropica  
Listeria  
Measles virus  
Mycoplasma  
Papillomavirus  
Pestivirus  
Picornaviridae  
Plasmodium berghei  
Plasmodium falciparum  
Plasmodium malariae  
Plasmodium ovale  
Plasmodium vivax  
Pneumocystis  
Pneumocystis carinii  
Poxviridae  
Pseudomonas  
RNA viruses  
Respiratory syncytial virus  
Retroviridae  
Rhinovirus  
Rubivirus  
Salmonella  
Shigella  
Staphylococcus  
Streptococcus  
Togaviridae

Toxoplasma  
Toxoplasma gondii  
Trichomonas  
Trichomonas vaginalis  
Trypanosoma  
Trypanosoma brucei  
Trypanosoma cruzi  
Trypanosoma gambiense  
Trypanosoma rhodesiense  
Vibrio  
Yersinia  
    (treatment of immunodysregulation condition caused by infection with;  
    incensole and furanogermacrens and compds. as antitumor and  
    antimicrobial agents)

IT Corticosteroids, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
    (treatment of immunodysregulation condition caused by treatment with;  
    incensole and furanogermacrens and compds. as antitumor and  
    antimicrobial agents)

IT Nucleoside analogs  
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL  
    (Biological study); USES (Uses)  
    (treatment of immunodysregulation condition caused by treatment with;  
    incensole and furanogermacrens and compds. as antitumor and  
    antimicrobial agents)

IT Immunosuppressants  
Mycosis  
Protozoa  
Wound  
    (treatment of immunodysregulation condition caused by; incensole and  
    furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Arthritis  
Asthma  
Autoimmune disease  
Cachexia  
Cirrhosis  
Diabetes mellitus  
Diarrhea  
Multiple sclerosis  
Respiratory distress syndrome  
    (treatment of; incensole and furanogermacrens and compds. as antitumor  
    and antimicrobial agents)

IT Antigens  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
    (tumor-assocd., drug targeting with monoclonal antibody to; incensole  
    and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Hematopoietic precursor cell  
    (tumors; incensole and furanogermacrens and compds. as antitumor and  
    antimicrobial agents)

IT Cytotoxic agents  
    (tyrophostins, pharmaceutical formulation further including; incensole  
    and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems  
    (vaginal; incensole and furanogermacrens and compds. as antitumor and  
    antimicrobial agents)

IT Infection  
    (viral, treatment of immunodysregulation condition caused by; incensole  
    and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Disease, animal  
    (wasting, treatment of; incensole and furanogermacrens and compds. as  
    antitumor and antimicrobial agents)

IT Interferons  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
 (.alpha., n1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.alpha., n3, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.alpha., pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.alpha.-2a, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.alpha.-2b, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lactams  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.beta.-, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.beta.1, a, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.gamma., 1b, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 37221-79-7, Vasoactive intestinal peptide  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (antagonist, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9002-06-6, Thymidine kinase  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 505-60-2, Mustard  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (anticancer, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 7585-39-9, .beta.-Cyclodextrin 7585-39-9D, .beta.-Cyclodextrin, hydroxypropyl derivs. 10016-20-3, .alpha.-Cyclodextrin 12619-70-4, Cyclodextrin 17465-86-0, .gamma.-Cyclodextrin  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (as pharmaceutical carrier; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 80-62-6, Methyl methacrylate 2867-47-2, (2-Dimethylaminoethyl) methacrylate 9004-38-0, Cellulose acetate phthalate 34346-01-5, Poly(lactic acid-glycolic acid) 441015-98-1  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (enteric coating of; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 121749-39-1  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 54-47-7D, Pyridoxal phosphate, reaction products with Hb conjugates  
 76-49-3, Bornyl acetate 80-57-9, Verbenone 87-44-5, .beta.-Caryophyllene 88-84-6, .beta.-Guaiene 99-49-0, Carvone 99-83-2, .alpha.-Phellandrene 99-87-6, p-Cymene 112-14-1, Octyl acetate 123-35-3, Myrcene 473-11-0, Eudesmane 489-80-5, Guaiane 495-61-4, .beta.-Bisabolene 502-61-4, Farnesene 507-70-0, Borneol 511-59-1, .beta.-Santalene 512-61-8, .alpha.-Santalene 515-12-8, Elemene 523-47-7, .beta.-Cadinene 555-10-2, .beta.-Phellandrene 562-74-3, Terpinen-4-ol 1335-14-4 1674-08-4, trans-Pinocarveol 1820-09-3, trans-Verbenol 2867-05-2, .alpha.-Thujene 3856-25-5, .alpha.-Copaene 4602-84-0, Farnesol 5208-59-3, .beta.-Bourbonene 6753-98-6, Humulene 6895-56-3, .beta.-Bergamotene 7663-66-3, Bergamotane 8007-35-0, Terpinyl acetate 8013-00-1, Terpinene 10178-38-8, Echinodol 14998-63-1D, Rhenium-186, etidronate complexes, biological studies 17627-44-0, .alpha.-Bisabolene 18794-84-8, .beta.-Farnesene 19912-61-9, Furanodiene 20479-06-5, .beta.-Ylangene 21698-66-8, Incensole oxide 21698-67-9, Incensole oxide acetate 22419-74-5, Incensole 25269-16-3, Isocembrene 25322-68-3D, conjugates with pyridoxylated Hb 28028-64-0, Germacrene 29063-28-3, Octanol 29350-73-0, Cadinene 31570-39-5, Cembrene-A 34701-53-6 35731-88-5, Isoincensole oxide 67921-02-2, Cembrenol 94325-73-2 94325-73-2D, compds. 122537-31-9, Oplopane 441771-56-8, Isoincensole 441771-57-9, Isoincensole acetate 441771-74-0, SKB 4  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 141436-78-4, Protein kinase C  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitor, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 52660-18-1, Casein kinase 1 366806-33-9, Casein kinase 2  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors (ICOS), pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 144114-21-6, HIV-1 Protease  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors, pharmaceutical formulation further contg.; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 70-18-8, Glutathione, biological studies 9030-21-1, Purine nucleoside phosphorylase 9040-48-6, Gelatinase 79747-53-8, Protein tyrosine phosphatase 79955-99-0, Stromelysin 80449-02-1, Tyrosine kinase 106096-93-9, Basic fibroblast growth factor 120178-12-3, Telomerase 131384-38-8, Ras farnesyltransferase 140879-24-9, Proteasome 141256-52-2, Matrilysin 141907-41-7, Matrix metalloproteinase 375798-61-1, Phosphatase, phosphoprotein  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 10102-43-9, Nitric oxide, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (modulators, pharmaceutical formulation further including; incensole and furanogermacrene and compds. as antitumor and antimicrobial agents)
- IT 9002-61-3, Chorionic gonadotrophin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

(monoclonal antibody to human, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9068-38-6, Reverse transcriptase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (nonnucleoside inhibitors of, pharmaceutical formulation further contg.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 1406-18-4, Vitamin E

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oil, as pharmaceutical carrier; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 54-05-7, Chloroquine 54-42-2, Idoxuridine 60-54-8, Tetracycline 69-74-9, Cytarabine Hydrochloride 70-00-8, Trifluridine 80-08-0, Dapsone 90-34-6, Primaquine 100-33-4, Pentamidine 130-95-0, Quinine 443-48-1, Metronidazole 494-79-1, Melarsoprol 665-66-7, Amantadine Hydrochloride 1501-84-4, Rimantadine Hydrochloride 1910-68-5, Methisazone 3056-17-5, d4T 3736-81-0, Diloxanide furoate 5536-17-4, Vidarabine 7481-89-2, DdC 8064-90-2 9004-70-0, HE-2000 10500-82-0, Famotidine Hydrochloride 10540-97-3, Memotidine Hydrochloride 11006-77-2, Statolon 15176-29-1, Edoxudine 15185-43-0, DOTC 19387-91-8, Tinidazole 19885-51-9, Aranotin 22994-85-0, Benznidazole 23256-30-6, Nifurtimox 25526-93-6, Alovudine 27591-69-1, Tilorone Hydrochloride 27762-78-3, Kethoxal 29984-33-6, Vidarabine Phosphate 30516-87-1, AZT 35607-20-6, Avridine 36791-04-5, Ribavirin 36983-81-0, Fosfonet Sodium 37338-39-9 39809-25-1, Penciclovir 51867-87-9 53230-10-7, Mefloquine 56219-57-9, Arildone 59277-89-3, Acyclovir 63198-97-0, Viroxime 63585-09-1, Foscarnet Sodium 63968-64-9D, Artemisinin, derivs. 68693-30-1, Somantadine Hydrochloride 69123-90-6, Fiacitabine 69123-98-4, Fialuridine 69655-05-6, DdI 69657-51-8, Acyclovir Sodium 69756-53-2, Halofantrine 72301-78-1, Zinviroxime 72301-79-2, Enviroxime 73514-87-1, Fosarilate 77181-69-2, Sorivudine 80883-55-2, Enviradene 82410-32-0, Ganciclovir 84408-37-7, Desciclovir 85087-20-3, Doxycycline 87495-31-6, Disoxaril 95233-18-4, Atovaquone 100817-46-7, Stibogluconic acid 104227-87-4, Famciclovir 106362-32-7, Peptide T 106941-25-7, PMEA 107910-75-8, Ganciclovir Sodium 110042-95-0, Acemannan 110143-10-7, Lodenosine 113852-37-2, Cidofovir 124436-59-5, Pirodavidir 124832-27-5, Valacyclovir Hydrochloride 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129618-40-2, Nevirapine 132210-43-6, Cipamfylline 134678-17-4, 3TC 136470-78-5, Abacavir 136817-59-9, Delavirdine 137487-62-8, Alvircept Sudotox 138540-32-6, Ateviridine Mesylate 141204-94-6, Co-artemether 142340-99-6 142632-32-4, Calanolide A 143491-57-0, Coviracil 145514-04-1, DAPD 147127-20-6, Tenofovir 147221-93-0, Delavirdine Mesylate 147318-81-8, KNI-272 147362-57-0, Loviride 149845-06-7, Saquinavir Mesylate 149950-60-7, Emivirine 150378-17-9, Indinavir 153127-49-2, ALX40-4C 154598-52-4, DMP 266 155148-31-5, AMD 3100 155213-67-5, Ritonavir 156879-70-8 159519-65-0, Pentafuside 159989-64-7, Nelfinavir 163451-80-7 170020-61-8, FP-21399 174484-41-4, Tipranavir 177932-89-7, DMP-450 178979-85-6, AG 1549 185220-03-5, PNU142721 192725-17-0, ABT-378 214287-88-4, DPC961 216863-66-0, L-756423 251562-00-2, T-1249 383198-56-9, BW 141 383198-57-0, BMS-232630 383198-58-1, PRO 542

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical formulation further contg.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 50-18-0, Cyclophosphamide 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-21-8, Fluorouracil 51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-19-0, Mitotane 53-43-0, DHEA 53-79-2, Puromycin 54-71-7, Pilocarpine hydrochloride 54-91-1, Pipobroman 55-21-0D, Benzamide,

N-substituted compds. 55-86-7, Mechlorethamine Hydrochloride 55-86-7D,  
 Nitrogen mustard, derivs. 55-98-1, Busulfan 56-53-1,  
 Diethylstilbestrol 57-22-7, Vincristine 57-63-6, Ethinyl oestradiol  
 57-83-0, Progesterone, biological studies 58-05-9, Leucovorin 58-58-2,  
 Puromycin Hydrochloride 59-05-2, Methotrexate 66-75-1, Uracil Mustard  
 83-89-6, Acridine 101-60-0, Porphyrin 106-60-5, Aminolevulinic acid  
 114-70-5, Sodium phenylacetate 122-79-2, Phenylacetate 125-45-1,  
 Azetepa 125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea 143-67-9,  
 Vinblastine Sulfate 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3,  
 Melfalan 154-42-7, Thioguanine 154-93-8, Carmustine 302-49-8,  
 Uredea 302-79-4, Tretinoin 305-03-3, Chlorambucil 320-67-2,  
 Azacitidine 359-83-1, Pentazocine 364-62-5, Metoclopramide 366-70-1,  
 Procarbazine Hydrochloride 378-44-9, Betamethasone 423-55-2,  
 Perflubron 459-86-9, Mitoguanine 465-65-6, Naloxone 472-15-1,  
 Betulinic acid 481-29-8, Epiandrosterone 518-28-5, Podophyllotoxin  
 520-85-4, Medroxyprogesterone 521-12-0, Dromostanolone Propionate  
 536-59-4, Perillyl alcohol 548-04-9, Hypericin 566-48-3, Formestane  
 569-57-3, Chlorotrianisene 578-95-0D, Acridone, imidazo derivs.  
 578-95-0D, Acridone, propylbis derivs. 595-33-5, Megestrol Acetate  
 645-05-6, Altretamine 646-08-2, .beta.-Alethine 671-16-9, Procarbazine  
 801-52-5, Porfiromycin 865-21-4, Vinblastine 911-45-5, Clomifene  
 968-93-4, Testolactone 1271-19-8, Titanocene dichloride 1402-81-9,  
 Ambomycin 1403-47-0, Duazomycin 1403-99-2, Mitogillin 1404-00-8,  
 Mitomycin 1404-15-5, Nogalamycin 1404-20-2, Peliomycin 1404-64-4,  
 Sparsomycin 1661-29-6, Meturedopa 1972-08-3, Dronabinol 1980-45-6,  
 Benzodepa 2068-78-2, Vincristine Sulfate 2353-33-5, Decitabine  
 2608-24-4, Piposulfan 2809-21-4D, Etidronic acid, rhenium-186 complexes  
 2919-66-6, Melengestrol acetate 2998-57-4, Estramustine 2998-57-4D,  
 Estramustine, analogs 3073-59-4, Hexamethylene bisacetamide 3094-09-5,  
 Doxifluridine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 3930-19-6,  
 Streptonigrin 4105-38-8 4291-63-8, Cladribine 4342-03-4, Dacarbazine  
 4342-07-8 4803-27-4, Anthramycin 5072-26-4, Buthionine sulfoximine  
 5373-42-2, Thaliblastine 5508-58-7, Andrographolide 5579-27-1,  
 Simtrazene 5581-52-2, Thiamiprine 5696-17-3, Epipropidine 6157-87-5,  
 Trestolone Acetate 7281-31-4, Vinglycin Sulfate 7440-06-4D,  
 Platinum, lipophilic compds. or complexes 7440-06-4D, Platinum, triamine  
 complexes 7644-67-9, Azotomycin 7689-03-4D, Camptothecin, derivs.  
 7724-76-7, Riboprine 7761-45-7, Metoprine 8052-16-2, Cactinomycin  
 9002-71-5, Thyroid-stimulating hormone 9014-02-2, Zinostatin  
 9014-42-0, Thrombopoietin 9014-42-0D, Thrombopoietin, mimetics  
 9015-68-3, Asparaginase 9027-98-9 9041-93-4, Bleomycin Sulfate  
 9050-67-3, Sizofiran 10043-49-9, Gold-198, biological studies  
 10087-89-5, Enpromate 10318-26-0, Mitolactol 10403-51-7, Mitindomide  
 10540-29-1, Tamoxifen 11002-22-5, Apurinic acid 11029-06-4, Elemene  
 11043-98-4, Mitocromin 11043-99-5, Mitomalcin 11056-06-7, Bleomycin  
 11056-12-5, Cirolemycin 11056-14-7, Mitocarcin 11056-15-8, Mitosper  
 12713-07-4D, Verdin, compds. 13010-47-4, Lomustine 13311-84-7,  
 Flutamide 13494-90-1, Gallium nitrate 13665-88-8, Mopidamol  
 13909-09-6, Semustine 14769-73-4, Levamisole 15475-56-6, Methotrexate  
 Sodium 15639-50-6, Safingol 15663-27-1, Cisplatin 17021-26-0,  
 Calusterone 17902-23-7, Tegafur 18378-89-7, Plicamycin 18416-85-8,  
 Lombricine 18556-44-0, Vinrosidine Sulfate 18588-57-3, Etoprine  
 18883-66-4, Streptozocin 19916-73-5, O6-Benzylguanine 20098-14-0,  
 Idramantone 20537-88-6, Amifostine 20638-84-0, Retinamide  
 20830-81-3, Daunorubicin 21059-48-3, Veramine 21679-14-1, Fludarabine  
 22668-01-5, Etanidazole 23214-92-8, Doxorubicin 23541-50-6,  
 Daunorubicin Hydrochloride 23593-75-1, Clotrimazole 24280-93-1,  
 Mycophenolic Acid 24584-09-6, Dexrazoxane 25316-40-9, Adriamycin  
 27302-90-5, Oxisuran 27314-97-2, Tirapazamine 27548-93-2D, Baccatin  
 III, derivs. 27686-84-6, Masoprocol 29069-24-7, Prednimustine  
 29767-20-2, Teniposide 30303-65-2, Docosanol 30387-51-0, Asperlin  
 30868-30-5, Pyrazofurin 31430-18-9, Nocodazole 31441-78-8,  
 Mercaptopurine 32954-58-8, Ipomeanol 33069-62-4,

**Paclitaxel 33069-62-4D, Paclitaxel, analogs**

and derivs. 33419-42-0, Etoposide 35301-24-7, Cedefingol 35846-53-8, Maytansine 35943-35-2, Triciribine 36508-71-1, Zorubicin Hydrochloride 37717-21-8, Flurocitabine 38270-90-5, Strontium Chloride Sr 89 38321-02-7, Dexverapamil 39325-01-4, Picibanil 40391-99-9, Pamidronic acid 41575-94-4, Carboplatin 41729-52-6, Dezaguanine 41992-22-7, Spirogermanium Hydrochloride 42228-92-2, Acivicin 42616-25-1, Methioninase 50264-69-2, Lonidamine 51264-14-3, Amsacrine 51321-79-0, Sparfosic acid 52128-35-5, Trimetrexate 52205-73-9, Estramustine Phosphate Sodium 52794-97-5, Carubicin Hydrochloride 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 54081-68-4, Vinleurosine Sulfate 54824-17-8, Mitonafide 55435-65-9, Acodazole Hydrochloride 56390-09-1, Epirubicin Hydrochloride 56420-45-2, Epirubicin 56605-16-4, Spiromustine 56741-95-8, Bropirimine 57381-26-7, Irsogladine 57576-44-0, Aclarubicin 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57852-57-0, Idamycin 57998-68-2, Diaziquone 58066-85-6, Miltefosine 58525-82-9, Azatyrosine 58957-92-9, Idarubicin 58970-76-6, Ubenimex 59653-73-5, Teroxirone 59917-39-4, Vindesine Sulfate 59989-18-3, 5-Ethynyluracil 60084-10-8, Tiazofurin 60203-57-8, Prostaglandin J2 60940-34-3, Ebselen 61825-94-3, Oxaliplatin 61966-08-3, Triciribine Phosphate 62304-98-7, Thymalfasin 62435-42-1, Perfosfamide 62488-57-7 62816-98-2, Ormaplatin 62928-11-4, Iproplatin 63590-19-2, Balanol 63612-50-0, Nilutamide 63950-06-1, Esorubicin Hydrochloride 65057-90-1, Talisomycin 65093-40-5, Cytarabine ocfosfate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 65222-35-7, Pazelliptine 65271-80-9, Mitoxantrone 65646-68-6, Fenretinide 65807-02-5, Goserelin 65886-71-7, Fazarabine 66569-27-5, Sparfosate Sodium 66849-34-1, Dexifosfamide 67699-41-6, Vinzolidine Sulfate 68278-23-9, Eflornithine Hydrochloride 68475-42-3, Anagrelide 69839-83-4, Didox 70052-12-9, Eflornithine 70384-29-1, Peplomycin Sulfate 70476-82-3, Mitoxantrone Hydrochloride 70641-51-9, Edelfosine 70711-40-9, Ametantrone Acetate 71294-60-5, Rohitukine 71439-68-4, Bisantrene Hydrochloride 71486-22-1, Vinorelbine 71522-58-2, Forfenimex 71628-96-1, Menogaril 72238-02-9D, Retelliptine, demethyl derivs. 72496-41-4, Pirarubicin 72629-69-7, Sarcophytol A 72732-56-0, Piritrexim 72741-87-8, Swainsonine 73105-03-0, Pentamustine 74149-70-5, Parabactin 74349-48-7, Mutamycin 74381-53-6, Leuprolide Acetate 74790-08-2, Spiroplatin 75219-46-4, Atrimustine 75330-75-5, Lovastatin 75607-67-9, Fludarabine Phosphate 75775-33-6D, Purpurin, compds. 75957-60-7, Splenopentin 76932-56-4, Nafarelin 77016-85-4, Plomestane 77327-05-0, Didemnin B 77599-17-8, Panomifene 77858-21-0, Velaresol 78113-36-7, Romurtide 78186-34-2, Bisantrene 79778-41-9, Neridronic acid 79831-76-8, Castanospermine 80451-05-4, Cecropin B 80576-83-6, Edatrexate 80663-95-2 80841-47-0, Asulacrine 81424-67-1, Caracemide 81965-43-7, SarCNU 82230-03-3, Carbetimer 82413-20-5, Droloxifene 82707-54-8, Neutral endopeptidase 82855-09-2D, Combretastatin, analogs 82952-64-5, Trimetrexate Glucuronate 83086-73-1, Tubulozole Hydrochloride 83150-76-9, Octreotide 83200-11-7, Vinepidine Sulfate 83519-04-4, Ilmofosine 83997-75-5, Iododoxorubicin 84030-84-2, Telluopyrylium 84088-42-6, Roquinimex 84371-65-3, Mifepristone 84412-94-2, Ruboxyl 85465-82-3, Thymotrinan 85622-93-1, Temozolomide 85754-59-2, Ambamustine 85969-07-9, Budotitane 85977-49-7, Tauromustine 86976-56-9, Betaclamycins 87005-03-6, Panaxytriol 87434-82-0, Dezaguanine Mesylate 87806-31-3, Porfimer Sodium 87810-56-8, Fostriecin 87860-39-7, Fostriecin Sodium 88303-60-0, Losoxantrone 88303-61-1, Losoxantrone Hydrochloride 89565-68-4, Tropisetron 89778-26-7, Toremfifene 89778-27-8, Toremfifene Citrate 90357-06-5, Bicalutamide 90996-54-6, Rhizoxin 92047-76-2, Tetrachlorodecaoxide 92118-27-9, Fotemustine

92788-10-8, Rogletimide 92803-82-2, Aphidicolin glycinate 94079-80-8,  
 Cicaprost 95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 95933-72-5,  
 Amidox 96201-88-6, Brequinar Sodium 96301-34-7, Atamestane  
 96346-61-1, Onapristone 96389-68-3, Crisnatol 96389-69-4, Crisnatol  
 Mesylate 96392-96-0, Dexormaplatin 96892-57-8, Hepsulfam 97068-30-9,  
 Elsamitrucin 97534-21-9, Merbarone 97682-44-5, Irinotecan  
 97752-20-0, Droloxifene Citrate 97919-22-7 98319-26-7, Finasteride  
 98383-18-7, Ecomustine 98631-95-9, Sobuzoxane 99009-20-8,  
 Pyrazoloacridine 99011-02-6, Imiquimod 99283-10-0, Molgramostim  
 99614-02-5, Ondansetron 100286-90-6, Irinotecan Hydrochloride  
 100324-81-0, Lisofylline 102396-24-7, Jasplakinolide 102676-31-3,  
 Fadrozole Hydrochloride 102676-47-1, Fadrozole 102822-56-0,  
 Mannostatin A 103222-11-3, Vapreotide 103612-80-2 104493-13-2,  
 Adecyphenol 105118-12-5, Piroxantrone Hydrochloride 105149-04-0,  
 Osaterone 105615-58-5, Oxaunomycin 105844-41-5, Plasminogen activator  
 inhibitor 106096-93-9D, Basic Fibroblast growth factor, saporin  
 conjugates 106400-81-1, Lometrexol 107000-34-0, Zanoterone  
 107256-99-5, Tamoxifen methiodide 107868-30-4, Exemestane 108736-35-2,  
 Lanreotide 108852-90-0, Nemorubicin 109837-67-4, Cycloplatan  
 110267-81-7, Amrubicin 110311-27-8, Sulofenur 110314-48-2, Adozelesin  
 110690-43-2, Emitefur 110942-02-4, Aldesleukin 110942-08-0, Luprolide  
 111490-36-9, Ziniplatin 111523-41-2, Enloplatin 112515-43-2, Topsentin  
 112522-64-2, Acetyldinaline 112809-51-5, Letrozole 112859-71-9,  
 Fluasterone 112887-68-0, Raltitrexed 112965-21-6, Calcipotriol  
 114084-78-5, Ibandroic acid 114285-68-6, Lentinan sulfate  
 114517-02-1, Fosquidone 114977-28-5, Taxotere 115150-59-9, Antagonist  
 G 115308-98-0, Tallimustine 115566-02-4, Bistratene A 115575-11-6,  
 Liarozole 115956-12-2, Dolasetron 116057-75-1, Idoxifene  
 117048-59-6, Combretastatin A4 117091-64-2, Etoposide Phosphate  
 118292-40-3, Tazarotene 119169-78-7, Epristeride 119413-54-6,  
 Topotecan Hydrochloride 119813-10-4, Carzelesin 120287-85-6,  
 Cetorelix 120408-07-3, Lometrexol Sodium 120500-15-4, Leinamycin  
 120511-73-1, Anastrozole 120685-11-2, Benzoylstauroporine  
 121181-53-1, Filgrastim 121263-19-2, Calphostin C 121288-39-9,  
 Loxoribine 121547-04-4, Mirimostim 122111-03-9, Gemcitabine  
 Hydrochloride 122341-38-2, Temoporfin 122431-96-3 122898-63-9,  
 Phenazinomycin 123040-69-7, Azasetron 123258-84-4, Itasetron  
 123760-07-6, Zinostatin stimalamer 123774-72-1, Sargramostim  
 123830-79-5, Teloxantrone Hydrochloride 123948-87-8, Topotecan  
 124012-42-6, Galocitabine 124689-65-2D, Cryptophycin A, derivs.  
 124784-31-2, Erbulozole 124904-93-4, Ganirelix 125317-39-7,  
 Vinorelbine Tartrate 125392-76-9, Acylfulvene 125533-88-2, Mofarotene  
 126297-39-0, Lissoclinamide 7 126443-96-7, Napavin 127984-74-1,  
 Lanreotide Acetate 128505-88-4, Naphterpin 128768-09-2, Placatin A  
 128768-11-6, Placatin B 129497-78-5, Verteporfin 129564-92-7, Azatoxin  
 129655-21-6, Bizelesin 129731-10-8, Vorozole 130167-69-0, Pegaspargase  
 130288-24-3, Duocarmycin SA 130364-39-5, Rubiginone B1 130370-60-4,  
 Batimastat 131190-63-1, Saintopin 132036-88-5, Ramosetron  
 132073-72-4, Tetrastomine 133432-71-0, Peldesine 134088-74-7,  
 Nartograstim 134381-30-9, Conagenin 134523-84-5 134633-29-7,  
 Tecogalan Sodium 134861-62-4, Dioxamycin 135257-45-3, Crambescidin 816  
 135381-77-0, Flezelastine 135383-02-7, Stipiamide 135558-11-1,  
 Lobaplatin 135819-69-1 135968-09-1, Lenograstim 137018-54-3,  
 Okicenone 137099-09-3, Turosteride 137219-37-5, Dehydrodidemnin B  
 137647-92-8, Axinastatin 1 137964-32-0 139755-79-6, Safingol  
 Hydrochloride 140207-93-8, Pentosan polysulfate sodium 140703-49-7,  
 Meterelin 142880-36-2, Ilomastat 144885-51-8, Sodium borocaptate  
 144916-42-7, Sonermin 145124-30-7, Bisnafide dimesylate 145858-50-0,  
 Liarozole Hydrochloride 146426-40-6, Flavopiridol 148317-76-4, Oracin  
 148584-53-6 148717-58-2, Palauamine 148717-90-2, Squalamine  
 149204-42-2, Kahalalide F 149260-80-0, Mycaperoxide B 149355-77-1,  
 Lamellarin-N triacetate  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL



(Biological study); USES (Uses)  
 (pharmaceutical formulation further including; incensole and  
 furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 149633-91-0, Leptolstatin 149715-96-8, Spongistatin 1 149882-10-0,  
 Lurtotecan 150829-93-9, Nisamycin 151272-78-5, Antarelix  
 152923-56-3, Dacliximab 153723-34-3, Axinastatin 2 153723-35-4,  
 Axinastatin 3 154039-60-8, Marimastat 154229-19-3, Abiraterone  
 154248-96-1, Iroplact 154277-21-1, Cypemycin 154361-50-9, Capecitabine  
 155233-30-0, Curacin A 156586-89-9, Edrecolomab 156790-85-1, Variolin  
 B 156856-30-3, Cytostatin 157078-48-3, Isohomohalichondrin B  
 157857-21-1, Maspin 158792-24-6, Collismycin A 158792-25-7,  
 Collismycin B 168482-36-8, Cryptophycin 8 172793-30-5 173046-02-1,  
 Thiocoraline 174305-65-8, Breflate 181887-82-1, Nitrullin  
 188364-40-1, CARN 700 200139-38-4, Suradista 212894-59-2, Pentrozole  
 246252-04-0, Lutetium texaphyrin 246252-06-2, Gadolinium texaphyrin  
 284041-10-7 324740-00-3, Vitaxin 441070-87-7, 1,2,3-  
 Triazolecarboxamide 441070-88-8 441070-92-4 441772-39-0,  
 Isobengazole 441772-43-6, Nagrestip 441772-66-3, Vinxaltine  
 441772-81-2, Sulfmosine 441774-07-8, Spicamycin D 441774-77-2,  
 Solverol  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (pharmaceutical formulation further including; incensole and  
 furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 60529-76-2, Thymopoietin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (receptor agonists, pharmaceutical formulation further including;  
 incensole and furanogermacrens and compds. as antitumor and  
 antimicrobial agents)

IT 79217-60-0, Cyclosporin  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (treatment of immunodysregulation condition caused by treatment with;  
 incensole and furanogermacrens and compds. as antitumor and  
 antimicrobial agents)

IT 50-07-7, Mitomycin C 1397-89-3, Amphotericin B  
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (treatment of immunodysregulation condition caused by treatment with;  
 incensole and furanogermacrens and compds. as antitumor and  
 antimicrobial agents)

IT 120178-12-3, **Telomerase**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors, pharmaceutical formulation further including; incensole  
 and furanogermacrens and compds. as antitumor and antimicrobial agents)

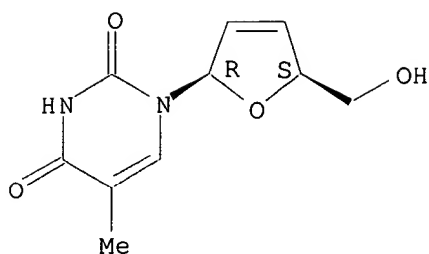
RN 120178-12-3 HCAPLUS  
 CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA  
 INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 3056-17-5, **d4T** 30516-87-1, **AZT**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (pharmaceutical formulation further contg.; incensole and  
 furanogermacrens and compds. as antitumor and antimicrobial agents)

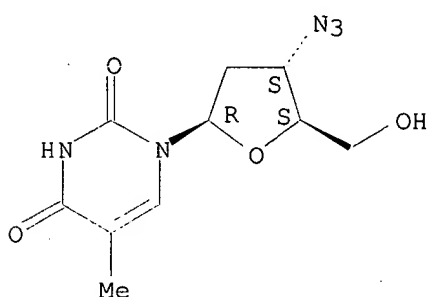
RN 3056-17-5 HCAPLUS  
 CN Thymidine, 2',3'-didehydro-3'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 30516-87-1 HCAPLUS  
 CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

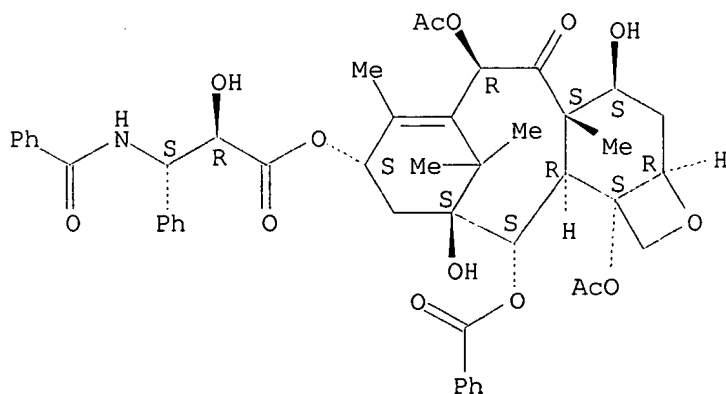
Absolute stereochemistry. Rotation (+).



IT 33069-62-4, Paclitaxel 33069-62-4D,  
 Paclitaxel, analogs and derivs.  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (pharmaceutical formulation further including; incensole and  
 furanogermacrens and compds. as antitumor and antimicrobial agents)

RN 33069-62-4 HCAPLUS  
 CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

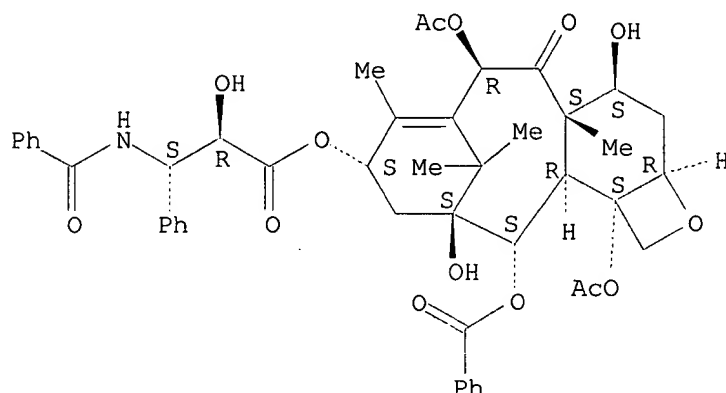
Absolute stereochemistry. Rotation (-).



RN 33069-62-4 HCAPLUS  
 CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

(2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis (acetyloxy)-12- (benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:494413 HCAPLUS

DN 135:207259

TI A quantitative assay of **telomerase** activity

AU Gan, Yuebo; Lu, Jie; Johnson, Andy; Wientjes, M. Guillaume; Schuller, David E.; Au, Jessie L.-S.

CS College of Pharmacy, The Ohio State University, Columbus, OH, 43210, USA

SO Pharmaceutical Research (2001), 18(4), 488-493

CODEN: PHREEB; ISSN: 0724-8741

PB Kluwer Academic/Plenum Publishers

DT Journal

LA English

CC 7-1 (Enzymes)

Section cross-reference(s): 14

AB Purpose: **Telomerase** is a ribonucleoprotein that extends telomeres at the ends of chromosome. Increased **telomerase** activity is assocd. with cellular immortality. The currently available assay for **telomerase**, i.e., telomeric repeat amplification protocol (TRAP), consists of 2 steps: (a) **telomerase**-mediated extension of an oligonucleotide primer by the enzyme-contg. exts. of cells and tissues, and (b) amplification of the **telomerase**-extended primer products by polymerase chain reaction (PCR) and detection of the PCR products. It is generally accepted that the current TRAP assay lacks quant. precision. The present study was to develop a quant. **telomerase** assay with greater precision and sensitivity. Methods: This new method used the primer extension method as in TRAP, plus the following modifications: (a) used a lysis buffer that yielded complete lysis of nuclei; (b) removal of PCR inhibitors by phenol/chloroform extn. after primer extension; and (c) used primers for the internal std. that were designed to reduce their competition with the **telomerase** products for PCR. Results: The modified method showed a good correlation ( $r^2 = 0.99$ ,  $P < 0.001$ ) between **telomerase** amt. (expressed as total protein in cell lysate) and its activity (expressed as **telomerase** products). Compared to the conventional TRAP, the new method (a) was more sensitive (av. of 5.5-fold in cultured cancer cells and >5.9-fold in patient tumors), (b) had a lower inter- and intra-day variability (>3-fold), and (c) showed a 2 to 4-fold broader range of linearity in the std. curve. The higher assay sensitivity further enabled the use of a non-radioactive method, i.e., ethidium bromide staining of

DNA, to detect the TRAP products, as opposed to the use of radioactive nucleotide and the more labor-intensive autoradiog. mandated by the conventional TRAP. Conclusion: We report here a quant. assay for **telomerase** activity in cultured human cancer cells and patient tumors.

ST **telomerase** detn modified TRAP assay; telomeric repeat amplification protocol modified detn **telomerase**

IT Genetic methods  
(TRAP (telomeric repeat amplification protocol), improved; quant. assay of **telomerase** activity using a modified telomeric repeat amplification protocol (TRAP))

IT Neoplasm  
(**telomerase** content; quant. assay of **telomerase** activity using a modified telomeric repeat amplification protocol (TRAP))

IT 120178-12-3, **Telomerase**  
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)  
(quant. assay of **telomerase** activity using a modified telomeric repeat amplification protocol (TRAP))

IT 1239-45-8, Ethidium bromide  
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
(staining; quant. assay of **telomerase** activity using a modified telomeric repeat amplification protocol (TRAP))

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Fu, W; J Biol Chem 1999, V274, P7264 HCAPLUS  
(2) Gelmini, S; Clin Chem 1998, V44, P2133 HCAPLUS  
(3) Hirose, M; Clin Chem 1998, V44, P2446 HCAPLUS  
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(11) Sun, D; Biochemistry 1999, V38, P4037 HCAPLUS  
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(13) Urquidi, V; Ann Rev Med 2000, V51, P65 HCAPLUS  
(14) Wright, W; Nucleic Acids Res 1995, V23, P3794 HCAPLUS  
(15) Wu, Y; Clin Chim Acta 2000, V293, P199 HCAPLUS

IT 120178-12-3, **Telomerase**  
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)  
(quant. assay of **telomerase** activity using a modified telomeric repeat amplification protocol (TRAP))

RN 120178-12-3 HCAPLUS

CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L65 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2002 ACS  
AN 2000:880951 HCAPLUS  
DN 134:37011  
TI Methods and compositions for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity  
IN Au, Jessie L.-S.; Wientjes, Guillaume  
PA USA  
SO PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM A61K031-00  
 CC 1-6 (Pharmacology)

Section cross-reference(s): 3, 7, 63

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE         |
|----|--|------|----------|-----------------|--------------|
| PI | WO 2000074667  | A2   | 20001214 | WO 2000-US15544 | 20000605 <-- |
|    | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,<br>CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,<br>ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,<br>LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,<br>SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA,<br>ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, KZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,<br>CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |              |

PRAI US 1999-137549P P 19990604 &lt;--

AB Methods and compns. are provided for modulating the activity of therapeutic agents for the treatment of a cancer by administering one or more agents that (either alone or in combination) induces **telomere** damage and inhibits **telomerase** activity in the cancer cell. The method initially uses, e.g., a **telomere** damage-inducing agent such as **paclitaxel**, and a **telomerase** inhibitory agent such as **AZT**. The invention also provides methods for identifying other agents with **telomere** damage-inducing activity and/or **telomerase** inhibitory activity (as well as and compns. having such activity), for use in the treatment of cancer.

ST antitumor **telomere** damage **telomerase** inhibition;  
**paclitaxel AZT telomere telomerase**  
 antitumor

IT **Nucleotides, biological studies**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(analogs; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT **Nucleic acids**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antisense; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT **Antitumor agents**

(bladder carcinoma; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT **Antitumor agents**

(brain; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT **Bladder**

(carcinoma, inhibitors; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT **Intestine, neoplasm**

(colon, inhibitors; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Antitumor agents  
(colon; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT DNA  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(complexes, with histones; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Drug delivery systems  
(controlled-release; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Gelatins, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(crosslinked; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Histones  
Nucleoproteins  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(deoxyribonucleohistones; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Liver, neoplasm  
(hepatoma, inhibitors; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Antitumor agents  
(hepatoma; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Nucleic acid hybridization  
(in situ, fluorescence; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Brain, neoplasm  
Lung, neoplasm  
Ovary, neoplasm  
Pancreas, neoplasm  
Testis, neoplasm  
Uterus, neoplasm  
(inhibitors; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Antitumor agents  
(leukemia; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Antitumor agents  
(lung; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Antitumor agents  
(mammary gland; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)

IT Antitumor agents  
Apoptosis  
Cytotoxic agents  
Drug delivery systems

Drug interactions  
Drug resistance  
Drug screening  
Extraction  
Fluorescent substances  
Hyperplasia  
Hypertrophy  
Nucleic acid hybridization  
PCR (polymerase chain reaction)  
Radiotherapy  
    **Telomeres** (chromosome)  
        (methods and compns. for modulating antitumor drug activity through  
          **telomere** damage, agent identification method, and method for  
          detecting **telomerase** activity)  
IT Primers (nucleic acid)  
Probes (nucleic acid)  
Radionuclides, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
    (methods and compns. for modulating antitumor drug activity through  
      **telomere** damage, agent identification method, and method for  
      detecting **telomerase** activity)  
IT Drug delivery systems  
    (microparticles; methods and compns. for modulating antitumor drug  
      activity through **telomere** damage, agent identification  
      method, and method for detecting **telomerase** activity)  
IT Drug delivery systems  
    (nanoparticles; methods and compns. for modulating antitumor drug  
      activity through **telomere** damage, agent identification  
      method, and method for detecting **telomerase** activity)  
IT Mammary gland  
Pharynx  
Prostate gland  
    (neoplasm, inhibitors; methods and compns. for modulating antitumor  
      drug activity through **telomere** damage, agent identification  
      method, and method for detecting **telomerase** activity)  
IT Antitumor agents  
    (ovary; methods and compns. for modulating antitumor drug activity  
      through **telomere** damage, agent identification method, and  
      method for detecting **telomerase** activity)  
IT Antitumor agents  
    (pancreas; methods and compns. for modulating antitumor drug activity  
      through **telomere** damage, agent identification method, and  
      method for detecting **telomerase** activity)  
IT Antitumor agents  
    (prostate gland; methods and compns. for modulating antitumor drug  
      activity through **telomere** damage, agent identification  
      method, and method for detecting **telomerase** activity)  
IT Drug delivery systems  
    (sustained-release; methods and compns. for modulating antitumor drug  
      activity through **telomere** damage, agent identification  
      method, and method for detecting **telomerase** activity)  
IT Drug interactions  
    (synergistic; methods and compns. for modulating antitumor drug  
      activity through **telomere** damage, agent identification  
      method, and method for detecting **telomerase** activity)  
IT Genetic methods  
    (**telomere** amt. and length assay (TALA); methods and compns.  
      for modulating antitumor drug activity through **telomere**  
      damage, agent identification method, and method for detecting  
      **telomerase** activity)  
IT Genetic methods  
    (**telomeric** repeat amplification protocol (TRAP); methods and  
      compns. for modulating antitumor drug activity through **telomere**

- damage, agent identification method, and method for detecting **telomerase** activity)
- IT Antitumor agents  
(testis; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT Antitumor agents  
(uterus; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 120178-12-3, **Telomerase**  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 3056-17-5, **d4T** 15663-27-1, **Cisplatin**  
30516-87-1, **AZT** 33069-62-4, **Paclitaxel**  
33069-62-4D, **Paclitaxel**, derivs.  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 9055-67-8 169592-56-7, **Caspase 3**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 67-66-3, **Chloroform**, miscellaneous 108-95-2, **Phenol**, miscellaneous  
123-51-3, **Isoamyl alcohol**  
RL: MSC (Miscellaneous)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 117490-04-7 125478-80-0 167976-62-7 167976-64-9 312653-01-3  
312653-02-4 312653-03-5 312653-04-6  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 9075-08-5, **Restriction endonuclease** 81295-18-3 81295-20-7, **Restriction endonuclease HhaI** 81295-23-0, **Restriction endonuclease HinfI**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 119456-37-0 156960-31-5, **DNA** (universal primer BB22) 182036-73-3  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for detecting **telomerase** activity)
- IT 120178-12-3, **Telomerase**  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(methods and compns. for modulating antitumor drug activity through **telomere** damage, agent identification method, and method for



detecting telomerase activity)  
 RN 120178-12-3 HCAPLUS  
 CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA INDEX NAME)

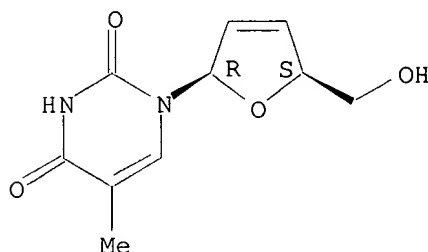
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IT 3056-17-5, d4T 30516-87-1, AZT  
 33069-62-4, Paclitaxel 33069-62-4D,  
 Paclitaxel, derivs.  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for modulating antitumor drug activity through telomere damage, agent identification method, and method for detecting telomerase activity)

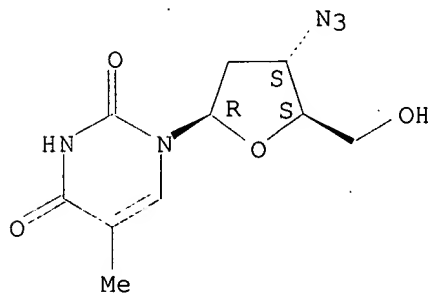
RN 3056-17-5 HCAPLUS  
 CN Thymidine, 2',3'-didehydro-3'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



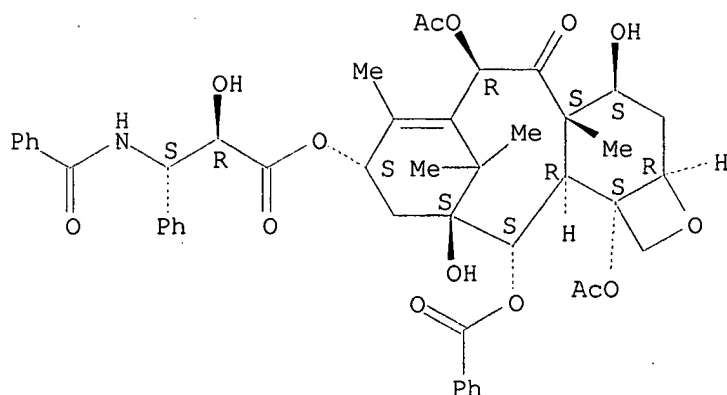
RN 30516-87-1 HCAPLUS  
 CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS  
 CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

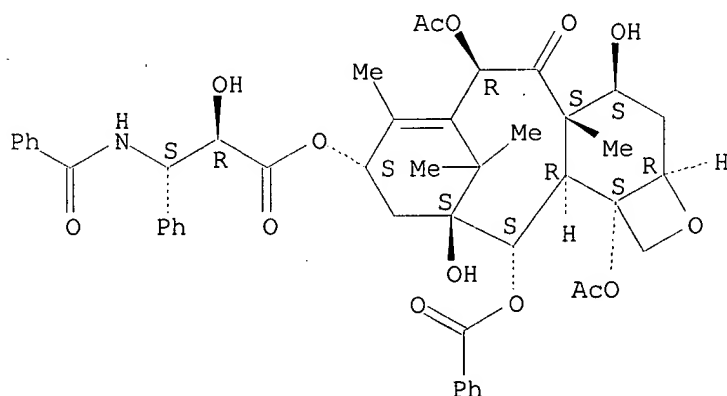
Absolute stereochemistry. Rotation (-).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,  
(2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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AN 2000:756717 HCAPLUS

DN 133:305589

TI Platinum complexes for the treatment of cancer and  
AIDS

IN Shaw, Jiajiu

PA Unitech Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

IC C07F015-00; A61K031-28

CC 1-6 (Pharmacology)

Section cross-reference(s): 63, 78

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE         |
|----|---|------|----------|-----------------|--------------|
| PI | WO 2000063219   | A1   | 20001026 | WO 2000-US10881 | 20000420 <-- |
|    | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,<br>CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, |      |          |                 |              |

ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,  
 LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
 SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,  
 AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6458832 B1 20021001 US 2000-552167 20000418 <--  
 US 2002165204 A1 20021107 US 2002-133117 20020425 <--  
 PRAI US 1999-130530P P 19990421 <--  
 US 2000-552167 A3 20000418

OS MARPAT 133:305589

AB The synthesis and use of a series of platinum **complexes** for the  
 treatment of **cancer** and AIDS are disclosed. The platinum  
**complexes** include cisplatin analogs, carboplatin analogs, and  
 cisplatin and folic acid compds.

ST platinum **complex** prepn **cancer** AIDS treatment;  
 cisplatin analog **cancer** AIDS treatment; carboplatin analog  
**cancer** AIDS treatment; folate cisplatin compd **cancer**  
 AIDS treatment

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Ad Elb; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (BRCAI; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Bad gene Harakiri; platinum **complexes** for treatment of  
**cancer** and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Bak; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Bax; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Bid; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Bik; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Bim; platinum **complexes** for treatment of **cancer**  
 and AIDS, and use with other agents)

IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

- (C-CAM; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Gene  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (ICE-CED3 protease; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Gene  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (MMAC1; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Gene, animal  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (RB1; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Gene, animal  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (TP53; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Phosphatidylserines  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (and phosphatidylserine carboxylates, platinum **complexes**; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Drug delivery systems  
(capsules; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Antitumor agents  
(colon **carcinoma**; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Intestine, neoplasm  
Intestine, neoplasm  
(colon, **carcinoma**, inhibitors; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Intestine, neoplasm  
Intestine, neoplasm  
(colon, inhibitors; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Antitumor agents  
(colon; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Gene  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (cytokine; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT DNA  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (damage, DNA damaging agents; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Adeno-associated virus  
Adenoviridae  
Herpesviridae  
Vaccinia virus  
(expression construct; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT DNA

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(genomic; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

IT Liver, **neoplasm**

Liver, **neoplasm**

(**hepatoma**, inhibitors; platinum **complexes** for treatment of **cancer** and AIDS)

IT **Antitumor agents**

(**hepatoma**; platinum **complexes** for treatment of **cancer** and AIDS)

IT Lung, **neoplasm**

Lung, **neoplasm**

Skin, **neoplasm**

Skin, **neoplasm**

(inhibitors; platinum **complexes** for treatment of **cancer** and AIDS)

IT Drug delivery systems

(injections, i.v.; platinum **complexes** for treatment of **cancer** and AIDS)

IT Drug delivery systems

(injections, s.c.; platinum **complexes** for treatment of **cancer** and AIDS)

IT Drug delivery systems

(injections; platinum **complexes** for treatment of **cancer** and AIDS)

IT Gamma ray

(irradn.; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

IT **Antitumor agents**

**Antitumor agents**

(lung; platinum **complexes** for treatment of **cancer** and AIDS)

IT **Antitumor agents**

(mammary gland; platinum **complexes** for treatment of **cancer** and AIDS)

IT Mammary gland

Mammary gland

Prostate gland

Prostate gland

(**neoplasm**, inhibitors; platinum **complexes** for treatment of **cancer** and AIDS)

IT Drug delivery systems

(oral; platinum **complexes** for treatment of **cancer** and AIDS)

IT Gene

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(p16; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

IT Gene

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(p21; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

IT Gene

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(p73; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

IT Drug delivery systems

(parenterals; platinum **complexes** for treatment of

- cancer** and AIDS)
- IT Anti-AIDS agents  
**Antitumor** agents  
 Drug delivery systems  
 (platinum **complexes** for treatment of **cancer** and AIDS)
- IT **Chemotherapy**  
 Gene therapy  
 Microwave  
 Radiotherapy  
 UV radiation  
 (platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Nucleic acids  
 Promoter (genetic element)  
 cDNA  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Amino acids, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (platinum **complexes**; platinum **complexes** for treatment of **cancer** and AIDS)
- IT **Antitumor** agents  
 (prostate gland; platinum **complexes** for treatment of **cancer** and AIDS)
- IT **Antitumor** agents  
**Antitumor** agents  
 (skin; platinum **complexes** for treatment of **cancer** and AIDS)
- IT **Antitumor** agents  
 (squamous cell **carcinoma**; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Surgery  
 (**tumor** resection; platinum **complexes** for treatment of **cancer** and AIDS)
- IT Radiotherapy  
 (x-ray; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Gene  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (zak1; platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)
- IT Amino acids, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.beta.-, platinum **complexes**; platinum **complexes** for treatment of **cancer** and AIDS)
- IT 296763-29-6P 296763-30-9P 302548-95-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (platinum **complexes** for treatment of **cancer** and AIDS)
- IT 7440-06-4D, Platinum, **complexes**, biological studies  
 15663-27-1, Cisplatin 41575-94-4, Carboplatin 74868-20-5 302547-77-9 302549-67-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(platinum **complexes** for treatment of **cancer** and AIDS)

IT 50-18-0, Cyclophosphamide 50-76-0, Dactinomycin 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 52-53-9, Verapamil 55-98-1, Busulfan 57-22-7, Vincristin 59-05-2, Methotrexate 148-82-3, Melphalan 305-03-3, Chlorambucil 518-28-5, Podophyllotoxin 671-16-9, Procarbazine 865-21-4, Vinblastin 1404-00-8, Mitomycin 3778-73-2, Ifosfamide 7689-03-4, Camptothecin 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-20-3, Nitrosurea 14913-33-8, Transplatin 18378-89-7, Plicamycin 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 30516-87-1, AZT 33069-62-4, Taxol 33419-42-0, Etoposide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

IT 60-18-4, L-Tyrosine, reactions 112-24-3 10025-99-7, Potassium tetrachloroplatinum (II) 25148-93-0, N,N'-Bis(2-dimethylaminoethyl)oxamide

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; platinum **complexes** for treatment of **cancer** and AIDS)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Hydes; US 4228090 A 1980 HCAPLUS
- (2) McClay; US 5844001 A 1998 HCAPLUS
- (3) Miller; Inorganica Chimica Acta 1999, V290(2), P237 HCAPLUS
- (4) Shaw; US 5922689 A 1999 HCAPLUS

IT 30516-87-1, AZT 33069-62-4, Taxol

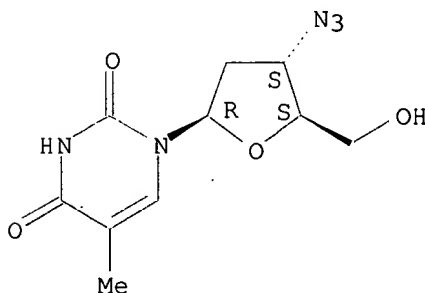
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(platinum **complexes** for treatment of **cancer** and AIDS, and use with other agents)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

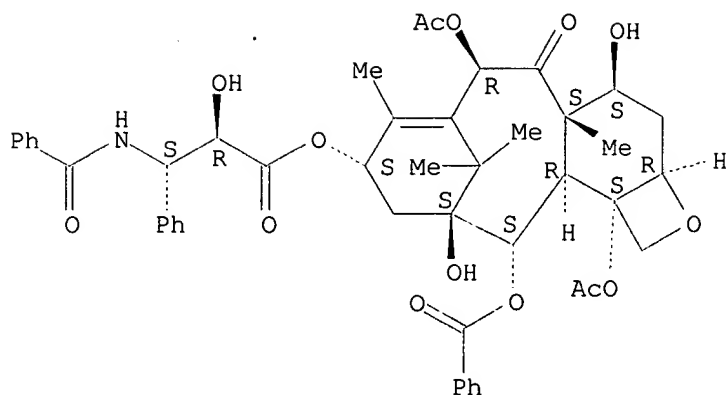
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.- (benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis (acetyloxy)-12- (benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:535357 HCAPLUS

DN 133:144904

TI Caspase cascade-based methods for identifying therapeutically effective antineoplastic agents, compounds so identified, and pharmaceutical compositions

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PA Cytovia, Inc., USA

SO PCT Int. Appl., 87 pp.

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DT Patent

LA English

IC ICM G01N033-48

ICS C12Q001-00

CC 1-6 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

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|---|------|--------------|-----------------|--------------|
| WO 2000045165   | A1   | 20000803     | WO 2000-US2329  | 20000201 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |      |              |                 |              |
| EP 1151295  | A1   | 20011107     | EP 2000-907081  | 20000201 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |              |                 |              |
| PRAI US 1999-118102P  | P    | 19990201 <-- |                 |              |
| US 1999-454595  | A    | 19991207 <-- |                 |              |
| WO 2000-US2329  | W    | 20000201     |                 |              |
| AB A method for identifying potentially therapeutically effective antineoplastic compds. comprises detg. the ability of test compds. to act as activators of the caspase cascade in viable cultured eukaryotic cells having an intact cell membrane and expressing a cancer phenotype, wherein a test compd. that enhances caspase cascade activity is detd. to have potential therapeutic efficacy. The method specifically differentiates activators of the caspase cascade from non-specific cell poisons. A therapeutic method useful to modulate in vivo apoptosis or in vivo neoplastic disease, comprising administering to a subject an effective amt. of a |      |              |                 |              |



compd. identified as a caspase cascade activator, is provided. Compds., pharmaceutical **compns.** and a kit for performing the therapeutic method are further provided.

ST **antitumor** agent screening caspase cascade

IT Gene, animal

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(BRCA1; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Gene, animal

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(Brca 2; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Animal cell line

(HL-60; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT **Antitumor** agents

**Antitumor** agents

(Hodgkin's disease inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT **Antitumor** agents

(Kaposi's **sarcoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Animal cell line

(PC-3; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Animal cell line

(T47D; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT **Antitumor** agents

(Wilms' **tumor**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Kidney, **neoplasm**

Kidney, **neoplasm**

(Wilms', inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Animal cell line

(ZR-75-1; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT **Antitumor** agents

(acute lymphocytic **leukemia**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Nervous system

(ataxia telangiectasia, ataxia telangiectasia mutated cells; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(bcl-2; caspase cascade-based methods for identifying therapeutically

- effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Gene, animal  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(bcr-c-abl; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(bladder **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
**Antitumor** agents  
(brain; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Carcinoid**  
(**carcinoid carcinoma** inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Adrenal cortex, **neoplasm**  
Bladder  
Bladder  
Esophagus  
Esophagus  
Head  
Head  
Lung, **neoplasm**  
Lung, **neoplasm**  
Mammary gland  
Mammary gland  
Neck, anatomical  
Neck, anatomical  
Ovary, **neoplasm**  
Ovary, **neoplasm**  
Pancreas, **neoplasm**  
Pancreas, **neoplasm**  
Prostate gland  
Prostate gland  
Stomach, **neoplasm**  
Stomach, **neoplasm**  
Testis, **neoplasm**  
Testis, **neoplasm**  
Thyroid gland, **neoplasm**  
Thyroid gland, **neoplasm**  
(**carcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(**carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Animal tissue culture  
**Antitumor** agents  
Apoptosis  
Chemiluminescent substances  
Color formers  
Drug delivery systems  
Drug screening  
Fluorescent substances  
Mutation

Permeation **enhancers**

## Polycythemia vera

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Natural products

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT p53 (protein)

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Multidrug resistance

(cells; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Antitumor agents

(cervix **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Uterus, **neoplasm**Uterus, **neoplasm**

(cervix, **carcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Chorion

## Chorion

(**choriocarcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Antitumor agents

(**choriocarcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Antitumor agents

(chronic lymphocytic **leukemia**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Antitumor agents

(chronic myelocytic **leukemia**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Antitumor agents

(colon **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Intestine, **neoplasm**Intestine, **neoplasm**

(colon, **carcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

## IT Antitumor agents

(endometrium **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT Uterus, **neoplasm**Uterus, **neoplasm**

- (endometrium, **carcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(esophagus **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Mycosis  
Mycosis  
(fungoides, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
**Antitumor agents**  
(genitourinary tract **tumor** inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(hairy cell **leukemia**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(head **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Brain, **neoplasm**  
Brain, **neoplasm**  
Hodgkin's disease  
Hodgkin's disease  
Skin, **neoplasm**  
Skin, **neoplasm**  
(inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Pancreatic islet of Langerhans  
Pancreatic islet of Langerhans  
(**insulinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(**insulinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(lung **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(lung small-cell **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(mammary gland **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(mammary gland; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(**melanoma**; caspase cascade-based methods for identifying

- therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT DNA repair  
(mismatch, DNA mismatch repair-deficient cells; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(multiple myeloma; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Mycosis  
Skin, **neoplasm**  
Skin, **neoplasm**  
(mycosis fungoides, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(mycosis fungoides; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(myelogenous leukemia, acute; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(neck carcinoma; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Mammary gland  
Mammary gland  
Prostate gland  
Prostate gland  
(**neoplasm**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Nerve, **neoplasm**  
Nerve, **neoplasm**  
(**neuroblastoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(**neuroblastoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(non-Hodgkin's lymphoma; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Bone, **neoplasm**  
(**osteosarcoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor** agents  
(ovary carcinoma; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT Cyclin dependent kinase inhibitors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(p16INK4; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

- IT **Antitumor agents**  
(pancreas **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Macroglobulins**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(primary macroglobulinemia; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Drug delivery systems**  
(prodrugs; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(prostate **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(prostate gland; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Kidney, neoplasm**  
**Kidney, neoplasm**  
(renal cell **carcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(renal cell **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(**rhabdomyosarcoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(**sarcoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
**Antitumor agents**  
(skin; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Lung, neoplasm**  
**Lung, neoplasm**  
(small-cell **carcinoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(soft tissue **sarcoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Animal tissue**  
**Animal tissue**  
(soft, **sarcoma**, inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)
- IT **Antitumor agents**  
(stomach **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents,

- comps. so identified, and pharmaceutical **compsns.**)
- IT Drug interactions  
(**synergistic**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, comps. so identified, and pharmaceutical **compsns.**)
- IT **Antitumor** agents  
(testis **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, comps. so identified, and pharmaceutical **compsns.**)
- IT Platelet (blood)  
(thrombocytosis, essential; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, comps. so identified, and pharmaceutical **compsns.**)
- IT **Antitumor** agents  
(thyroid gland **carcinoma**; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, comps. so identified, and pharmaceutical **compsns.**)
- IT Urogenital tract  
Urogenital tract  
(**tumor** inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, comps. so identified, and pharmaceutical **compsns.**)
- IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-32-8, Benzo[a]pyrene, biological studies 50-44-2, Mercaptopurine 50-76-0, Actinomycin D 51-21-8, 5-Fluorouracil 51-28-5, 2,4-Dinitrophenol, biological studies 51-75-2, Mechlorethamine 53-79-2, Puromycin 54-05-7, Chloroquine 54-31-9 54-62-6, Aminopterin 54-64-8, Thimerosal 54-92-2, Iproniazid 55-98-1, Busulfan 56-12-2, .gamma.-Aminobutyric acid, biological studies 56-25-7, Cantharidin 56-49-5, 3-Methylcholanthrene 56-75-7, Chloramphenicol 57-24-9, Strychnine 57-62-5 58-00-4, Apomorphine 59-05-2, Methotrexate 60-38-8, Strophanthidin acetate 62-74-8, Sodium fluoroacetate 64-77-7, Tolbutamide 64-86-8, Colchicine 66-27-3, Methylmethane sulfonate 66-28-4, Strophanthidin 66-76-2, Dicoumarol 66-81-9, Cycloheximide 71-63-6, Digitoxin 73-31-4, Melatonin 76-28-8, Sarmentogenin 81-23-2, Dehydrocholic acid 82-10-0D, derivs. 83-79-4, Rotenone 83-89-6, Quinacrine 84-17-3, Dienestrol 84-65-1, Anthraquinone 90-65-3, Penicillic acid 97-44-9, Acetarsol 97-77-8, Disulfiram 100-33-4, Pentamidine 115-02-6, Azaserine 121-19-7, Roxarsone 121-54-0, Benzethonium chloride 123-03-5, Cetylpyridinium chloride 126-07-8, Griseofulvin 127-07-1, Hydroxyurea 129-20-4, Oxyphenbutazone 136-77-6, Hexylresorcinol 143-67-9, Vinblastine sulfate 147-94-4, Cytarabine 148-82-3, Melphalan 152-11-4, Verapamil hydrochloride 154-42-7, Thioguanine 302-27-2, Aconitine 305-03-3, Chlorambucil 306-37-6 314-03-4, Pimethixene 316-42-7, Emetine hydrochloride 320-67-2, 5-Azacytidine 446-86-6, Azathioprine 474-07-7 476-32-4, Chelidonine 481-39-0, Juglone 482-53-1, Osajin 483-18-1, Emetine 484-29-7, Dictamine 498-95-3, Nipecotic acid 508-64-5D, Strophanthidin acid, derivs. 508-77-0, Cymarin 514-42-1 518-28-5, Podophyllotoxin 518-28-5D, Podophyllotoxin, derivs. 518-75-2, Citrinin 543-90-8, Cadmium acetate 548-19-6, Isoginkgetin 548-62-9, Gentian violet 564-25-0, Doxycycline 572-03-2, Pomiferin 595-05-1, Calycanthine 630-56-8, Hydroxyprogesterone caproate 630-60-4, Ouabain 865-21-4, Vinblastine 979-32-8, Estradiol valerate 1134-47-0, Baclofen 1254-85-9, Cedrelone 1397-89-3, Amphotericin B 1397-94-0, Antimycin a 1400-61-9, Nystatin 1404-88-2, Tyrothricin 1405-20-5, Polymyxin B sulfate 1405-87-4, Bacitracin 1405-97-6, Gramicidin 1449-05-4, 18.alpha.-Glycyrrhetic acid 1915-67-9D, Mexicanolide, derivs. 1951-25-3, Amiodarone 2524-37-0 2582-86-7, Atrovenetin 2631-92-7 2752-65-0, Gambogic acid 2752-65-0D, Gambogic acid, derivs. 2753-30-2D, Gedunin, derivs. 3094-09-5, 5-Fluoro-5'-deoxyuridine 3902-71-4, Trioxsalen 4342-03-4, Dacarbazine 4360-12-7, Ajmaline 5490-46-0, Lonchocarpic acid diacetate 5914-82-9 5996-03-2

6385-58-6, Bithionolate sodium 7299-11-8, Psoromic acid 7689-03-4, Camptothecin 10410-83-0, Anthothecol 12244-57-4 12542-36-8, Gossypol-acetic acid 14923-17-2, Arcaine sulfate 15663-27-1, Cisplatin 16561-29-8, Phorbol myristate acetate 17046-60-5 17560-51-9, Metolazone 17617-45-7, Picrotoxinin 17754-44-8, Atractyloside 18000-24-3, 7-Chlorokynurenic acid 18883-66-4, Streptozocin 20004-62-0D, Resistomycin, derivs. 20315-68-8 20830-75-5, Digoxin 21105-15-7, Obtusaquinone 22144-77-0, Cytochalasin d 23214-92-8, Doxorubicin 23590-85-4 24280-93-1, Mycophenolic acid 26213-95-6 26927-01-5 28028-68-4, Crassin acetate 28789-35-7 28860-95-9, Carbidopa 30516-87-1, Zidovudine 30850-52-3, Decahydrogambogic acid 32476-67-8, Periplocymarin 33069-62-4, Taxol 33419-42-0, Etoposide 34157-83-0, Celastrol 41575-94-4, Carboplatin 42193-38-4 49842-07-1, Tobramycin sulfate 53179-09-2, Sisomicin sulfate 53179-11-6, Loperamide 62996-74-1, Staurosporine 64964-48-3, Sericetin diacetate 65059-09-8 66451-22-7, Chukrasin 69505-55-1 70904-56-2D, Kyotorphin, derivs. 70904-57-3D, derivs. 85967-06-2D, Rhodomyrtoxin, derivs. 141543-62-6 161804-20-2, Benzamil hydrochloride 286935-58-8 286935-60-2 287103-76-8 287103-77-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT 186322-81-6, Caspase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT 25535-16-4, Propidium iodide

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT 7440-70-2, Calcium, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**malignant** hypercalcemia inhibitors; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

IT 211918-90-0 220846-54-8 287376-78-7 287376-79-8 287376-80-1

287376-81-2 287376-82-3 287376-83-4 287376-84-5

RL: PRP (Properties)

(unclaimed sequence; caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and pharmaceutical **compns.**)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Fulda; Cancer Research 1997, V57, P4656

(2) Mohr; Proc Natl Acad Sci USA 1998, V95, P5045 HCAPLUS

(3) Qi; Oncogene 1997, V15, P1207 HCAPLUS

IT 30516-87-1, Zidovudine 33069-62-4,

Taxol

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(caspase cascade-based methods for identifying therapeutically effective **antineoplastic** agents, compds. so identified, and

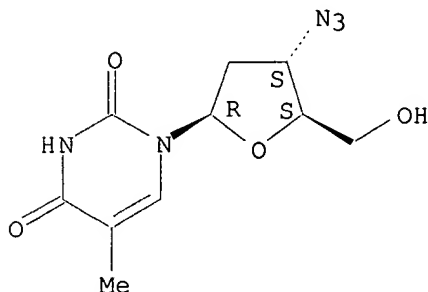


pharmaceutical compns.)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

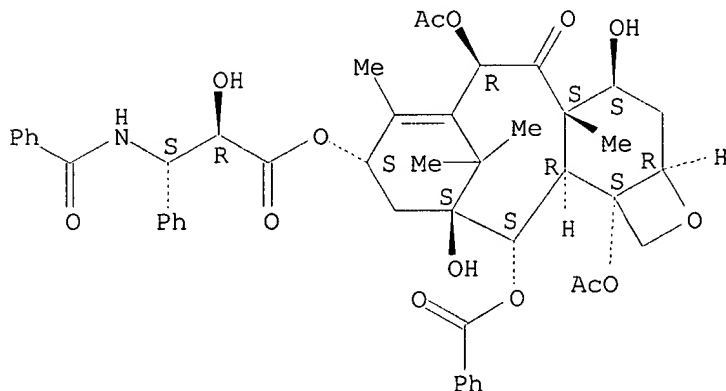
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:438177 HCAPLUS

DN 133:305333

TI Cell death in **paclitaxel**-dependent Chinese hamster ovary cells  
 is initiated by the loss of **telomeric** DNA repeats

AU Multani, Asha S.; Chandra, Joya; McConkey, David J.; Sen, Subrata; Cabral,  
 Fernando; Pathak, Sen

CS Departments of Cancer Biology, The University of Texas M. D. Anderson  
 Cancer Center, Houston, TX, 77030, USA

SO Oncology Research (1999), 11(10), 455-460

CODEN: ONREE8; ISSN: 0965-0407

PB Cognizant Communication Corp.

DT Journal

LA English

CC 1-6 (Pharmacology)

Section cross-reference(s): 13, 14

AB We have reported earlier that cell death in a metastatic murine melanoma  
 cell line induced by **paclitaxel** and its water-sol. conjugates is

mediated through the extensive erosion of **telomeric** repeats. The purpose of this study was to investigate if loss of **telomeric** repeats was also involved in cell death of Tax-18 and Tax-2-4, two **paclitaxel**-requiring mutant Chinese hamster ovary (CHO) cell lines. Tax-18 and Tax-2-4 cells were grown in **paclitaxel**-free culture medium for 24, 48, 72, and 96 h at 37.degree.C and then harvested for cytol. preps. Control cultures of both cell lines were grown in **paclitaxel**-supplemented medium and harvested simultaneously. We found that the frequency of **telomeric** assocns. in metaphase preps. was increased with the duration of **paclitaxel**-depleted culture; Tax-18 cells showed a higher incidence (33.0%) of endoreduplicated metaphases at 24 h of **paclitaxel**-depleted culture than did Tax-2-4 cells, in which endoreduplicated metaphases were rare; the frequency of polyploid cells was increased after 48, 72, and 96 h of **paclitaxel**-depleted culture for Tax-18 relative to that for Tax-2-4 cells; both cell lines showed redns. in **telomeric** signals at chromosomal termini, but not in the interphase nuclei; and both cell lines had shorter terminal **telomeric** restriction fragments after culture in **paclitaxel**-depleted medium. These results support our earlier observations and indicate that redn. of **telomeric** repeats is involved in G2/M cell arrest (endoreduplication) followed by severe DNA fragmentation, and then cell death of two CHO mutant cell lines that require **paclitaxel** for cell division.

ST cell death **paclitaxel** telomere DNA repeat

IT Interphase (cell cycle)

(G2-phase; cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

IT Cell death

**Telomeres** (chromosome)

(cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

IT Mitosis

(metaphase; cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

IT Repetitive DNA

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**telomeric**; cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

IT 33069-62-4, **Paclitaxel**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

IT 120178-12-3, **Telomerase**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 33069-62-4, **Paclitaxel**

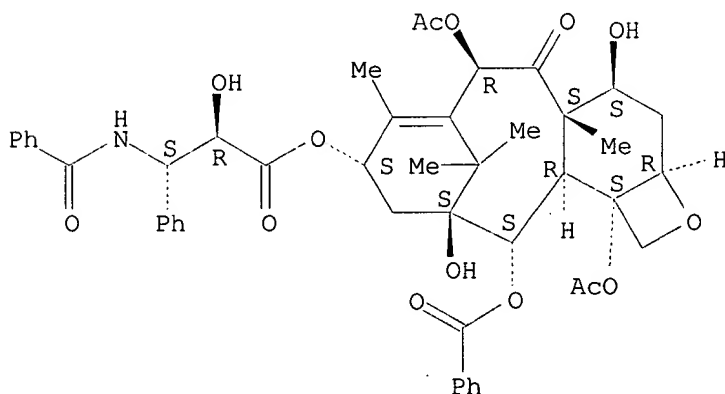
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.- (benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 120178-12-3, **Telomerase**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(cell death in **paclitaxel**-dependent Chinese hamster ovary cells is initiated by loss of **telomeric** DNA repeats)

RN 120178-12-3 HCAPLUS

CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L65 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:98300 HCAPLUS

DN 132:132356

TI Chemically induced intracellular hyperthermia for therapeutic and diagnostic use

IN Bachynsky, Nicholas; Roy, Woodie

PA Texas Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 149 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-06

CC 1-12 (Pharmacology)

Section cross-reference(s): 9, 63

FAN.CNT 1

|      | PATENT NO.  | KIND   | DATE         | APPLICATION NO. | DATE         |
|------|---|--|--------------|-----------------|--------------|
| PI   | WO 2000006143   | A1   | 20000210     | WO 1999-US16940 | 19990727 <-- |
|      | W:  | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |              |                 |              |
|      | RW:   | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |              |                 |              |
|      | CA 2337690  | AA   | 20000210     | CA 1999-2337690 | 19990727 <-- |
|      | AU 9951318  | A1   | 20000221     | AU 1999-51318   | 19990727 <-- |
|      | AU 750313   | B2   | 20020718     |                 |              |
|      | EP 1098641  | A1   | 20010516     | EP 1999-935949  | 19990727 <-- |
|      | R:  | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |              |                 |              |
| PRAI | US 1998-94286P  | P  | 19980727 <-- |                 |              |
|      | WO 1999-US16940   | W  | 19990727 <-- |                 |              |
| AB   | Therapeutic pharmacol. agents and methods are disclosed for chem. induction of intracellular hyperthermia and/or free radicals for the diagnosis and treatment of infections, <b>malignancy</b> , and other medical conditions. A process and <b>compn.</b> are provided for the diagnosis or killing of <b>cancer</b> cells and inactivation of susceptible bacterial, parasitic, fungal, and viral pathogens by chem. generating heat, and/or free radicals and/or hyperthermia-inducible immunogenic determinants by using mitochondrial uncoupling agents, esp. 2,4-dinitrophenol, and their <b>conjugates</b> , either alone or in <b>combination</b> with other drugs, hormones, cytokines and radiation. |  |              |                 |              |
| ST   | intracellular hyperthermia mitochondria uncoupler diagnosis therapy; dinitrophenol intracellular hyperthermia diagnosis therapy; <b>cancer</b> infection diagnosis therapy intracellular hyperthermia; <b>antitumor</b> antiinfective intracellular hyperthermia mitochondria uncoupler   |  |              |                 |              |
| IT   | Hepatitis   |  |              |                 |              |
|      | (C; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)   |  |              |                 |              |
| IT   | Imaging   |  |              |                 |              |
|      | (IR; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)  |  |              |                 |              |
| IT   | Lichen  |  |              |                 |              |
|      | (acids; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)   |  |              |                 |              |
| IT   | <b>Antitumor</b> agents   |  |              |                 |              |
|      | (adenocarcinoma; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)  |  |              |                 |              |
| IT   | Cell cycle  |  |              |                 |              |
|      | (agents specific for; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)   |  |              |                 |              |
| IT   | Antibiotics   |  |              |                 |              |
|      | (aminoglycoside; chem. induced intracellular hyperthermia for   |  |              |                 |              |

- diagnostic and therapeutic use, and use with other agents)
- IT Artery
  - (angioplasty; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Peptides, biological studies
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (antibiotic; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Macrolides
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (antibiotics; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Antibodies
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (antiviral; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Infection
  - (bacterial; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Mammary gland
  - (**carcinoma**; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Alkylating agents, biological
  - Anti-infective agents
  - Anti-ischemic agents
  - Antibacterial agents
  - Antitumor** agents
  - Antiviral agents
  - Combinatorial** chemistry
  - Combinatorial** library
  - Cyanine dyes
  - Diagnosis
  - Echinococcus multilocularis
  - Fungicides
  - Human immunodeficiency virus
  - Hyperthermia (therapeutic)
  - Infection
  - Lyme disease
  - Neoplasm**
  - Parasiticides
  - Positron-emission tomography
  - Radiotherapy
  - Surgery
    - (chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)
- IT Cytokines
  - Histones
  - Interleukin 1
  - Interleukin 10
  - Interleukin 2
  - Interleukin 4
  - Leukotrienes
  - Nucleoside analogs
  - Oligosaccharides, biological studies
  - Polyenes
  - Polyethers, biological studies
  - Prostaglandins

Sulfonamides  
Tetracyclines  
Thromboxanes  
Thyroid hormones

**Tumor** necrosis factors

Ubiquinones

Uncoupling protein

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Heat-shock proteins

Radicals, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Alcohols, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fluoro; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Neuroglia

(**glioma**; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Hormones, animal, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hormone agonists; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Antibodies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(humanized, to HER-2/neu; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Liver, disease

(hydatid; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Fungi

Parasite

(infection; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Antibiotics

Ionophores

(ionophorous antibiotic uncouplers; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Drug delivery systems

(liposomes; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Antibiotics

(macrolide; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Metabolism

(metabolic rate; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT Mitochondria

(mitochondrial uncoupling agents; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

- agents)
- IT neu (receptor)  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(monoclonal humanized antibodies to; chem. induced intracellular  
hyperthermia for diagnostic and therapeutic use, and use with other  
agents)
- IT Antibodies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(monoclonal, to HER-2/neu; chem. induced intracellular hyperthermia for  
diagnostic and therapeutic use, and use with other agents)
- IT Fatty acids, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(monounsaturated; chem. induced intracellular hyperthermia for diagnostic  
and therapeutic use, and use with other agents)
- IT Prostate gland  
Prostate gland  
(**neoplasm**, inhibitors; chem. induced intracellular  
hyperthermia for diagnostic and therapeutic use, and use with other  
agents)
- IT Alkaloids, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(podophyllin and plant; chem. induced intracellular hyperthermia for  
diagnostic and therapeutic use, and use with other agents)
- IT Fatty acids, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(polyunsaturated; chem. induced intracellular hyperthermia for diagnostic  
and therapeutic use, and use with other agents)
- IT **Antitumor** agents  
(prostate gland; chem. induced intracellular hyperthermia for  
diagnostic and therapeutic use, and use with other agents)
- IT Drugs  
(sulfa drugs; chem. induced intracellular hyperthermia for diagnostic  
and therapeutic use, and use with other agents)
- IT Drug interactions  
(**synergistic**; chem. induced intracellular hyperthermia for  
diagnostic and therapeutic use, and use with other agents)
- IT Animal tissue  
(target tissue metabolic rate; chem. induced intracellular hyperthermia  
for diagnostic and therapeutic use, and use with other agents)
- IT Fatty acids, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(unsaturated; chem. induced intracellular hyperthermia for diagnostic and  
therapeutic use, and use with other agents)
- IT Infection  
(viral; chem. induced intracellular hyperthermia for diagnostic and  
therapeutic use, and use with other agents)
- IT Interferons  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(.alpha.-2a; chem. induced intracellular hyperthermia for diagnostic  
and therapeutic use, and use with other agents)
- IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.alpha.-2b; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

# IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.alpha.; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

# IT Lactams

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.-, antibiotics; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

# IT Antibiotics

(.beta.-lactam; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

# IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

# IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.gamma.; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

# IT 9034-40-6, Luteinizing hormone-releasing factor

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(agonists; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT 50-18-0 50-49-7 50-65-7 50-76-0, Actinomycin D 51-21-8 51-28-5, biological studies 51-28-5D, derivs. and **conjugates** 51-48-9, biological studies 51-75-2 52-24-4 53-03-2 53-79-2 54-42-2 55-98-1 56-53-1 56-75-7 56-85-9, L-Glutamine, biological studies 57-22-7 57-62-5 57-63-6 57-92-1, biological studies 58-22-0 58-27-5 59-05-2D, analogs 59-87-0 60-33-3, 9,12-Octadecadienoic acid (9Z,12Z)-, biological studies 60-54-8D, derivs. 61-32-5 61-33-6, biological studies 61-68-7 61-73-4 63-74-1 63-74-1D, derivs. 65-49-6 66-79-5 67-20-9 67-45-8 68-35-9 68-81-5 70-00-8 72-14-0 74-81-7, biological studies 76-43-7 79-43-6D, nitrobenzene derivs 79-57-2 87-86-5 91-40-7 92-82-0D, Phenazine, derivs. 97-18-7 100-02-7, biological studies 102-82-9 103-82-2D, Benzeneacetic acid, derivs. 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 112-86-7 114-07-8, Erythromycin 116-44-9 125-84-8 126-07-8 127-33-3 147-85-3, L-Proline, biological studies 147-94-4 148-79-8 148-82-3 154-21-2 154-42-7 154-93-8 299-11-6 302-79-4, Retinoic acid 305-03-3 320-67-2 370-86-5 389-08-2 439-14-5 443-48-1 459-86-9 463-40-1 479-20-9 484-49-1 506-26-3 506-32-1 518-28-5 519-23-3 520-85-4 521-52-8 527-17-3 529-37-3D, 4(1H)-Quinolinone, derivs. 530-78-9 531-82-8 548-62-9 555-60-2 564-25-0 593-38-4 595-33-5 606-06-4 630-56-8 637-07-0 671-16-9 727-81-1 754-91-6 768-94-5, Tricyclo[3.3.1.1<sup>3,7</sup>]decan-1-amine 804-36-4 865-21-4, Vincalukoblastine 914-00-1 956-48-9 960-71-4 1041-01-6 1066-17-7, Colistin 1151-51-5 1392-21-8, Leucomycin 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1402-38-6, Actinomycin 1402-82-0, Amphomycin 1403-17-4, Candicidin 1403-66-3, Gentamicin 1404-04-2, Neomycin 1404-88-2, Tyrothricin 1405-87-4,



Bacitracin 1405-97-6, Gramicidin 1406-05-9, Penicillin 1406-11-7,  
 Polymyxin 1689-83-4 1960-88-9 2001-95-8, Valinomycin 2022-85-7  
 2030-63-9 2034-22-2 2338-10-5 2338-11-6 2338-12-7 2338-29-6  
 2520-21-0 3056-17-5 3511-16-8 3778-73-2 4151-50-2  
 4342-03-4 4428-95-9 4543-33-3 5331-91-9 5536-17-4 6217-54-5  
 6236-05-1 6893-02-3 7283-41-2 7440-43-9, Cadmium, biological studies  
 7440-70-2, Calcium, biological studies 7481-89-2 7562-61-0  
 8011-61-8, Tyrocidine 8052-16-2, Actinomycin C 9007-92-5, Glucagon,  
 biological studies 10118-90-8 10417-94-4 10461-11-7 10537-47-0  
 11000-17-2, Vasopressin 11003-38-6, Capreomycin 11006-76-1,  
 Virginiamycin 11006-78-3, Stendomycin 11017-50-8, Suzukacillin  
 11029-61-1, Gramicidin A 11056-06-7, Bleomycin 11111-23-2, Lividomycin  
 11115-82-5, Enduracidin 12633-72-6, Amphotericin 12692-85-2,  
 Antiamebin 13010-47-4 13278-36-9 13311-84-7 13392-28-4  
 13799-49-0 13799-49-0D, isomers 13909-09-6 13925-12-7 14459-29-1  
 14698-29-4 15663-27-1 16128-96-4 17090-79-8, Monensin 17650-86-1  
 17924-92-4 18323-44-9 19246-70-9 19562-30-2 19721-56-3  
 20559-55-1 22494-42-4 22662-39-1 22916-47-8 25104-18-1  
 25546-65-0 26097-80-3 26655-39-0 26786-84-5 26787-78-0  
 27061-78-5, Alamethicin 27138-57-4D, lactone, derivs. 27194-24-7D,  
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 30042-37-6 30516-87-1 31441-78-8, Purinethiol 32986-56-4  
 33069-62-4 33354-58-4 33419-42-0 34368-04-2 36791-04-5  
 36877-68-6D, derivs. 37231-28-0, Melittin 37517-28-5 38000-06-5  
 38640-92-5 40451-44-3 41575-94-4 45285-51-6 50892-23-4  
 51940-44-4 52214-84-3 53024-98-9, Everninomicin 53714-56-0  
 54965-21-8 55486-00-5 56219-57-9 59277-89-3 60842-45-7, Desaspidin  
 60976-67-2, Gramicidin J 61477-96-1 62362-59-8 63939-09-3, Curamycin  
 65277-42-1 65454-19-5, Trichotoxin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT 68786-66-3 69655-05-6 72301-79-2 74011-58-8 74722-67-1  
 80738-43-8D, Lincosamide, derivs. 80802-79-5, Cecropin (antibacterial peptide) 81627-83-0, Colony-stimulating factor 1 82410-32-0  
 82419-36-1 83150-76-9 83869-56-1, Colony-stimulating factor 2  
 84625-61-6 85721-33-1 86386-73-4 89107-47-1, Hypelcin 91156-71-7  
 95233-18-4 100292-37-3, Zervamicin 113041-69-3, Magainin 115717-83-4  
 121007-17-8 127779-20-8 128470-16-6 134678-17-4 136470-78-5  
 145781-92-6 148159-85-7, Saturnisporin SA IV 150378-17-9 154598-52-4  
 155213-67-5 159989-64-7 161814-49-9 171980-70-4, Trichorzin HA V  
 256932-84-0 256932-84-0D, sulfoxide and sulfone metabolites  
 256932-85-1 256932-86-2 256932-87-3 256932-88-4 256932-89-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT 9001-92-7, Proteinase 9039-48-9, Aromatase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

IT 29656-58-4D, derivs.  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lichen acids; chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Gordon; US 4569836 A 1986 HCAPLUS

(2) Gordon; US 5622686 A 1997

(3) Rubin; US 5005588 A 1991

IT 3056-17-5 30516-87-1 33069-62-4

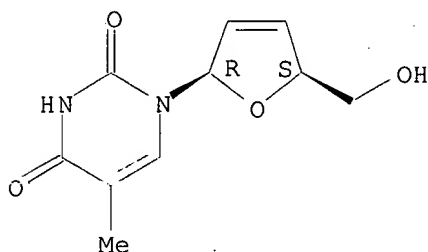
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chem. induced intracellular hyperthermia for diagnostic and therapeutic use, and use with other agents)

RN 3056-17-5 HCAPLUS

CN Thymidine, 2',3'-didehydro-3'-deoxy- (9CI) (CA INDEX NAME)

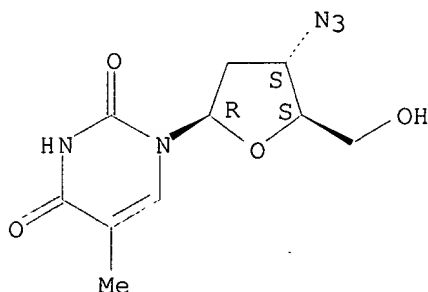
Absolute stereochemistry.



RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

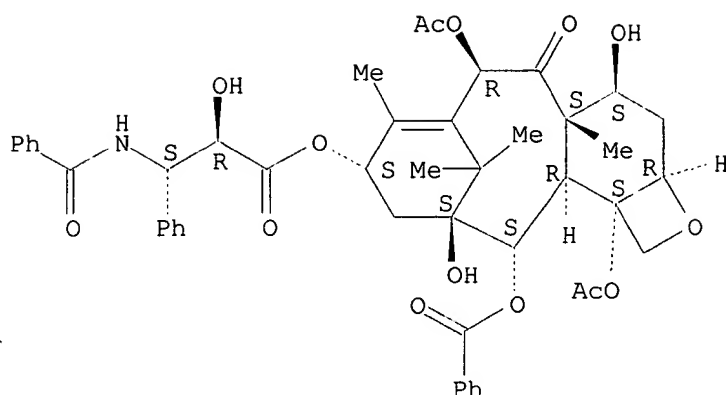
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:659252 HCAPLUS

DN 131:291291

TI New **combined** preparation for the treatment of **neoplastic** or infectious diseases

IN Bartholeyns, Jacques; Fournon, Yves; Romet-Lemonne, Jean-loup

PA I.D.M. Immuno-Designed Molecules, Fr.

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K035-14

ICS C12N005-08; A61K035-14; A61K031-00; A61K035-14; A61K038-19;

A61K035-14; A61K039-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 15

FAN.CNT 1

| PATENT NO.  | KIND  | DATE         | APPLICATION NO. | DATE         |
|---|---|--------------|-----------------|--------------|
| WO 9951248  | A1  | 19991014     | WO 1999-EP2105  | 19990329 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |   |              |                 |              |
| CA 2321029  | AA  | 19991014     | CA 1999-2321029 | 19990329 <-- |
| AU 9931479  | A1  | 19991025     | AU 1999-31479   | 19990329 <-- |
| EP 1067944  | A1  | 20010117     | EP 1999-913310  | 19990329 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |   |              |                 |              |
| JP 2002510639   | T2  | 20020409     | JP 2000-542019  | 19990329 <-- |
| PRAI EP 1998-400783   | A   | 19980402 <-- |                 |              |
| WO 1999-EP2105  | W   | 19990329 <-- |                 |              |
| AB The present invention relates to a <b>combined</b> prepn. contg. as active substance the following individual components, in the form of a kit-of-parts: monocyte derived cells, particularly cytotoxic macrophages, <b>chemotherapy</b> or immunotherapy drugs, for the <b>simultaneous</b> , sep. or <b>sequential</b> use, for the treatment of <b>cancer</b> or infectious diseases.   |   |              |                 |              |
| ST  | kit <b>antitumor</b> immunocyte immunostimulant |              |                 |              |
| IT  | Immunostimulants                                |              |                 |              |

- (adjuvants; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Glycosides  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (amino; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Blood transfusion  
 (apheresis; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Blood serum  
 (autologous; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Medical goods  
 (blood bags, collection with; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Monocyte  
 (cells derived from; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Blood  
 (centrifugation of; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Leukocyte  
 (collection of peripheral; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Lymphocyte  
 Mononuclear cell (leukocyte)  
 (collection of; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Intestine, **neoplasm**  
 (colorectal; **combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Antibiotics  
**Antitumor** agents  
 Antiviral agents  
 Culture media  
 Cytotoxic agents  
 Immunostimulants  
 Immunotherapy  
**Melanoma**  
 Mycobacterium BCG  
 Ovary, **neoplasm**  
 Test kits  
 Vaccines  
 (**combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Cytokines  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)  
 (**combined** prepn. for the treatment of **neoplastic** or infectious diseases)
- IT Anthracyclines  
 Cyclins  
 Interleukin 12  
 Interleukin 2  
 Macrolides  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (**combined** prepn. for the treatment of **neoplastic** or infectious diseases)

- IT Preservatives  
(cryo-; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Macrophage  
(cytotoxic; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Apoptosis  
(inducers; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Drug delivery systems  
(injections; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Lung, neoplasm  
(mesothelioma; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Glycopeptides  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PEP (Physical, engineering or chemical process); THU  
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(muramic acid-contg.; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Leukemia  
(myelogenous; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Prostate gland  
(**neoplasm**; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Centrifugation  
(of blood; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Amines, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(polyamines, nonpolymeric, inhibitors; **combined** prepn. for  
the treatment of **neoplastic** or infectious diseases)
- IT Proliferation inhibition  
(**proliferation** inhibitors; **combined** prepn. for the  
treatment of **neoplastic** or infectious diseases)
- IT Erythrocyte  
Platelet (blood)  
Polymorphonuclear leukocyte  
(removal of; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Vaccines  
Vaccines  
(**tumor**; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Antitumor agents  
Antitumor agents  
(vaccines; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Alkaloids, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PEP (Physical, engineering or chemical process); THU  
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(vinca; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Lactams  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PEP (Physical, engineering or chemical process); THU  
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(.beta.-; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)
- IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(.gamma.; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)

IT 124-38-9, Carbon dioxide, biological studies 7782-44-7, Oxygen, biological studies

RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)  
(artificial atm. contg.; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)

IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 51-21-8D, Fluorouracil, derivs. 57-22-7, Vincristine 71-58-9, Prodasone 154-93-8, Carmustine 156-54-7, Sodium butyrate 446-86-6, Azathioprine 1406-05-9, Penicillin 4428-95-9, Foscarnet 7803-58-9, Sulfamide 10540-29-1, Tamoxifen 11111-12-9, Cephalosporins 15663-27-1, Cisplatin 20830-81-3, Daunorubicin 25316-40-9, Adriamycin **30516-87-1, Azt**

**33069-62-4, Taxol** 37205-61-1, Proteinase inhibitor 59277-89-3, Acyclovir 63798-73-2, Cyclosporine 79517-01-4, Sandostatin 83869-56-1, Gmcsf 114977-28-5D, Taxotere, derivs. 143011-72-7, Gcsf  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**combined** prepn. for the treatment of **neoplastic** or infectious diseases)

IT 80449-01-0, Topoisomerase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; **combined** prepn. for the treatment of  
**neoplastic** or infectious diseases)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bartoleyns, J; IMMUNOBIOLOGY 1996, V195(4-5), P550 MEDLINE
- (2) Hennemann, B; CLINICAL IMMUNOTHERAPEUTICS 1996, V5/4, P294
- (3) Hennemann, B; JOURNAL OF IMMUNOTHERAPY 1997, V20(5), P365 HCAPLUS
- (4) I D M Immuno-Designed Molecules; WO 9622781 A 1996 HCAPLUS

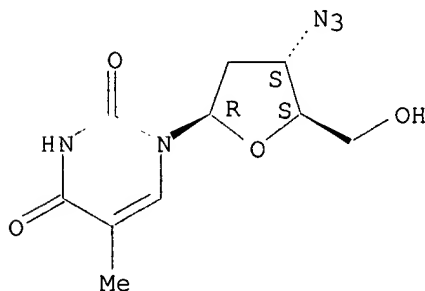
IT **30516-87-1, Azt 33069-62-4, Taxol**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**combined** prepn. for the treatment of **neoplastic** or infectious diseases)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

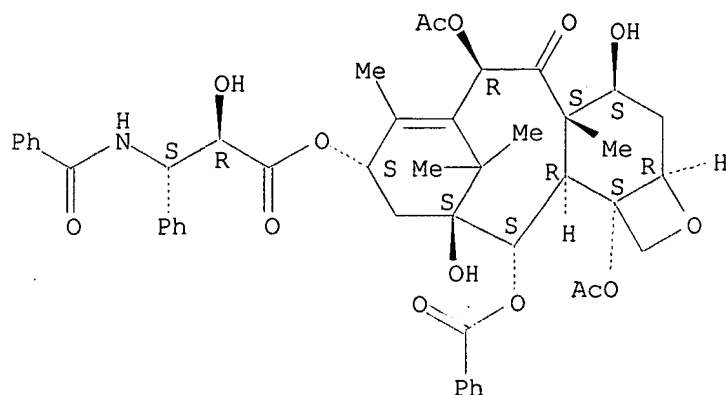


RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-

tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:606769 HCAPLUS

DN 131:341861

TI Pluronic P85 increases permeability of a broad spectrum of drugs in polarized BBMEC and Caco-2 cell monolayers

AU Batrakova, Elena V.; Li, Shu; Miller, Donald W.; Kabanov, Alexander V.

CS Department of Pharmaceutical Sciences, Nebraska Medical Center, College of Pharmacy, Omaha, NE, 68198-6025, USA

SO Pharmaceutical Research (1999), 16(9), 1366-1372

CODEN: PHREEB; ISSN: 0724-8741

PB Kluwer Academic/Plenum Publishers

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

AB Previous studies demonstrated that inhibition of P glycoprotein (P-gp) by Pluronic P85 (P85) block copolymer increases apical (AP) to basolateral (BL) transport of rhodamine 123 (R123) in the polarized monolayers of bovine brain microvessel endothelial cells (BBMEC) and Caco-2 cells. The present work examines the effects of P85 on the transport of fluorescein (Flu), doxorubicin (Dox), etoposide (Et), **taxol** (Tax), 3'-azido-3'-deoxythymidine (**AZT**), valproic acid (VPA) and loperamide (Lo) using BBMEC and Caco-2 monolayers as in vitro models of the blood brain barrier and intestinal epithelium resp. Drug permeability studies were performed on the confluent BBMEC and Caco-2 cell monolayers mounted in Side-Bi-Side diffusion cells. Exposure of the cells to P85 significantly **enhanced** AP to BL permeability coeffs. of Flu, Tax, Dox and **AZT** in both cell models. Further, P85 **enhanced** AP to BL transport of Et, VPA and Lo in Caco-2 monolayers. No changes in the permeability coeffs. of the paracellular marker mannitol were obsd. in the presence of the copolymer. P85 increases AP to BL permeability in BBMEC and Caco-2 monolayers with respect to a broad panel of structurally diverse compds., that were previously shown to be affected by P-gp and/or multidrug resistance assoc. protein (MRP) efflux systems. Broad specificity of the block copolymer effects with respect to drugs and efflux systems appears to be a valuable property in view of developing pharmaceutical formulations to increase drug accumulation in selected organs and overcome both acquired and intrinsic drug resistance that limits the effectiveness of many **chemotherapeutic** agents.

ST drug permeability Pluronic P35; **antitumor** drug permeability

- Pluronic P35
- IT Animal cell line  
(Caco-2; Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)
- IT Antitumor agents  
Biological transport  
Drug delivery systems  
Multidrug resistance  
(Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)
- IT P-glycoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)
- IT Brain  
(microvessel endothelial cells; Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)
- IT Biological transport  
(permeation; Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)
- IT 99-66-1, Valproic acid 2321-07-5, Fluorescein 23214-92-8, Doxorubicin 30516-87-1, Azt 33069-62-4, Taxol 33419-42-0, Etoposide 53179-11-6, Loperamide 106392-12-5, Pluronic P85  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (2) Batrakova, E; Br J Cancer 1996, V74, P1545 HCAPLUS
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- (18) Miller, D; J Tiss Cult Meth 1992, V14, P217
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- (24) Takasawa, K; J Pharmacol Exp Ther 1997, V281, P369 HCAPLUS
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- (26) Van Veen, H; Semin Cancer Biol 1997, V8, P183 HCAPLUS
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(30) Yu, V; Bioconjugate Chem 1996, V7, P209

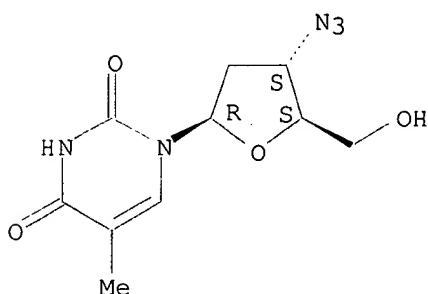
IT 30516-87-1, Azt 33069-62-4, Taxol

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (Pluronic P85 increases permeability of a broad spectrum of drugs in polarized bovine brain microvessel endothelial cells and Caco-2 cell monolayers)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

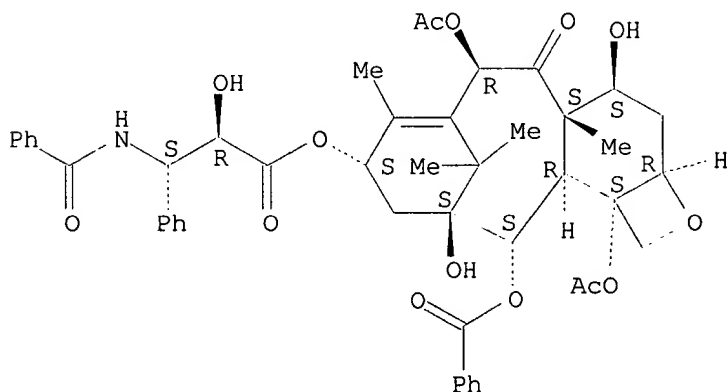
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:578949 HCAPLUS

DN 131:209112

TI A method for evaluating the antitumor effect of a drug or a treatment

IN Ishikawa, Atsuo; Yanaginuma, Yuji; Tsuruoka, Hiroki; Ito, Akira

PA Kayaku K. K., Japan; Pola Chemical Industries, Inc.

SO Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM C12Q001-527

CC 1-1 (Pharmacology)

Section cross-reference(s): 7

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE         |
|----|--|------|----------|-----------------|--------------|
| PI | JP 11243994  | A2   | 19990914 | JP 1998-52077   | 19980304 <-- |
| AB | A method is described for evaluating the antitumor effect of a drug or a treatment by measuring a change in <b>telomere</b> -related substance activity in cancer cells caused by the drug or treatment. By this method, the antitumor effect of a drug or a treatment, and the characteristics of cancer cells against the drug or treatment, can be evaluated. The method is also useful for predicting the effect of an antitumor agent in cancer chemotherapy. Correlations were obsd. between the growth inhibitory effect on cell lines derived from various types of cancer and the change in <b>telomerase</b> activity in these cells caused by the antitumor agent (e.g., cisplatin, <b>taxol</b> ). |      |          |                 |              |
| ST | antitumor agent cancer chemotherapy <b>telomerase telomere</b>   |      |          |                 |              |
| IT | Animal cell line<br>(SiHa; HeLa; SKOV3; method for evaluating antitumor effect of drug or treatment)   |      |          |                 |              |
| IT | Uterus, neoplasm<br>Uterus, neoplasm<br>(cervix, inhibitors; method for evaluating antitumor effect of drug or treatment)  |      |          |                 |              |
| IT | Antitumor agents<br>(cervix; method for evaluating antitumor effect of drug or treatment)  |      |          |                 |              |
| IT | Ovary, neoplasm<br>Ovary, neoplasm<br>(inhibitors; method for evaluating antitumor effect of drug or treatment)  |      |          |                 |              |
| IT | Antitumor agents<br>Chemotherapy<br><b>Telomeres</b> (chromosome)<br>(method for evaluating antitumor effect of drug or treatment)   |      |          |                 |              |
| IT | Antitumor agents<br>Antitumor agents<br>(ovary; method for evaluating antitumor effect of drug or treatment)   |      |          |                 |              |
| IT | <b>120178-12-3</b> , Nucleotidyltransferase, terminal deoxyribo-( <b>telomeric</b> DNA)<br>RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)<br>(method for evaluating antitumor effect of drug or treatment)  |      |          |                 |              |
| IT | <b>15663-27-1</b> , Cisplatin <b>33069-62-4</b> , <b>Taxol</b><br>RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)<br>(method for evaluating antitumor effect of drug or treatment)  |      |          |                 |              |
| IT | <b>120178-12-3</b> , Nucleotidyltransferase, terminal deoxyribo-( <b>telomeric</b> DNA)<br>RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)<br>(method for evaluating antitumor effect of drug or treatment)  |      |          |                 |              |
| RN | <b>120178-12-3</b> HCAPLUS   |      |          |                 |              |
| CN | Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA INDEX NAME)  |      |          |                 |              |

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

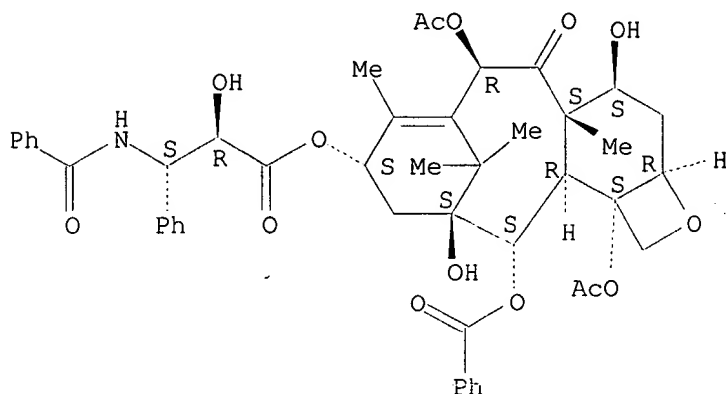
IT **33069-62-4**, **Taxol**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(method for evaluating antitumor effect of drug or treatment)

RN **33069-62-4** HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-

2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:312077 HCAPLUS

DN 130:346876

TI Potential interaction of antiretroviral therapy with **paclitaxel** in patients with AIDS-related Kaposi's **sarcoma**

AU Schwartz, J. D.; Howard, W.; Scadden, D. T.

CS New York Hosp./Cornell Med. Center Hematology/Oncology, New York, NY, 10021, USA

SO AIDS (London) (1999), 13(2), 283-284

RC607.A 24 A344

CODEN: AIDSET; ISSN: 0269-9370

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 1-4 (Pharmacology)

AB The interactions between cytochrome P 450 3A(CYP3A)-suppressive anti-HIV regimens and **paclitaxel** resulted in substantial **chemotherapy**-related side effects in patients with AIDS-related Kaposi's **sarcoma**. **Paclitaxel** (100 mg/m<sup>2</sup>) administration over 3 h every other week to patients with HIV infection and Kaposi's **sarcoma** resulted in near-total disappearance of Kaposi's **sarcoma**. The first 12 cycles were complicated only by mild nausea and alopecia; intermittent granulocyte colony-stimulating factor was used to prevent neutropenia. Antiretroviral therapy included several combinations of zidovudine, zalcitabine, lamivudine, stavudine, and indinavir, all of which were unsuccessful in reducing the viral load. Subsequently the patients were started on didanosine, saquinavir and delavirdine. As a result of this therapy, **paclitaxel** resulted in profound mucositis requiring hospitalization and febrile neutropenia with an abs. neutrophil count <100 x10<sup>6</sup>/l. Given the above scenario, it is likely, that coadministration of delavirdine and saquinavir results in a situation where levels of either (or both) drugs are increased and concomitant administration of taxane **chemotherapy** with **paclitaxel** leads to side-effects significantly out of proportion to the taxane dose used. Thus, taxane doses in these situations should be reduced and patients carefully monitored.

ST taxane **chemotherapy** adverse interaction antiretroviral therapy AIDS **sarcoma**; **paclitaxel** interaction adverse antiretroviral therapy AIDS **sarcoma**

IT Drug interactions

(adverse; potential interaction of antiretroviral therapy with  
**paclitaxel** in patients with AIDS-related Kaposi's  
**sarcoma**)

IT AIDS (disease)  
Antiviral agents  
(potential interaction of antiretroviral therapy with  
**paclitaxel** in patients with AIDS-related Kaposi's  
**sarcoma**)

IT Taxanes  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(potential interaction of antiretroviral therapy with  
**paclitaxel** in patients with AIDS-related Kaposi's  
**sarcoma**)

IT Antitumor agents  
(**sarcoma**; potential interaction of antiretroviral therapy  
with **paclitaxel** in patients with AIDS-related Kaposi's  
**sarcoma**)

IT 9035-51-2, Cytochrome P450, biological studies  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(3A antiretroviral therapy interaction with **paclitaxel** in  
patients with AIDS-related Kaposi's **sarcoma**)

IT 3056-17-5, Stavudine 7481-89-2, Zalcitabine  
8064-90-2 30516-87-1, Zidovudine 33069-62-4,  
**Paclitaxel** 69655-05-6, Didanosine 86386-73-4, Fluconazole  
127779-20-8, Saquinavir 134678-17-4, Lamivudine 136817-59-9,  
Delavirdine 150378-17-9, Indinavir 159989-64-7, Nelfinavir  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(potential interaction of antiretroviral therapy with  
**paclitaxel** in patients with AIDS-related Kaposi's  
**sarcoma**)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

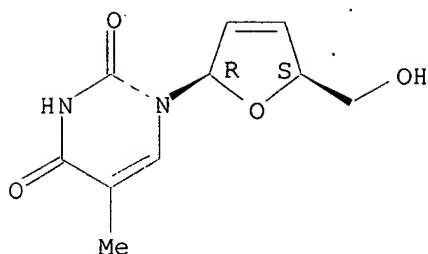
(1) Anon; Ann Intern Med 1998, V128, P1079  
(2) Carpenter, C; Ann Intern Med 1998, V128, P1057  
(3) Carpenter, C; JAMA 1998, V280, P78 HCAPLUS  
(4) Cresteil, T; Cancer Res 1994, V54, P386 HCAPLUS  
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(7) Harris, J; Cancer Res 1994, V15, P4026  
(8) Piscitelli, S; Clin Infect Dis 1996, V23, P685 HCAPLUS  
(9) von Moltke, L; J Clin Pharmacol 1998, V38, P106 HCAPLUS

IT 3056-17-5, Stavudine 30516-87-1,  
Zidovudine 33069-62-4, **Paclitaxel**  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(potential interaction of antiretroviral therapy with  
**paclitaxel** in patients with AIDS-related Kaposi's  
**sarcoma**)

RN 3056-17-5 HCAPLUS

CN Thymidine, 2',3'-didehydro-3'-deoxy- (9CI) (CA INDEX NAME)

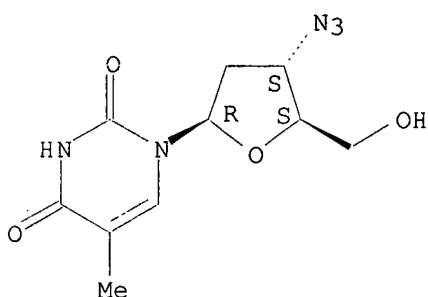
Absolute stereochemistry.



RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

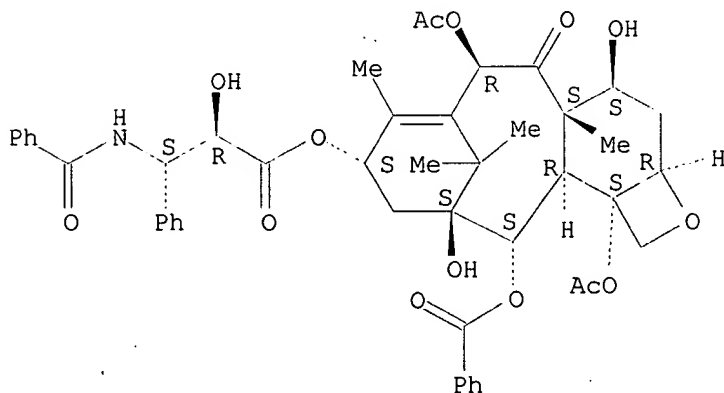
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:42002 HCAPLUS

DN 130:276313

TI Cell-killing by **paclitaxel** in a metastatic murine melanoma cell line is mediated by extensive **telomere** erosion with no decrease in **telomerase** activity

AU Multani, Asha S.; Li, Chun; Ozen, Mustafa; Imam, Ashraf S.; Wallace,

Sidney; Pathak, Sen  
 CS Department of Cancer Biology, The University of Texas M.D. Anderson Cancer  
 Center, Houston, TX, 77030, USA  
 SO Oncology Reports (1999), 6(1), 39-44  
 CODEN: OCRPEW; ISSN: 1021-335X  
 PB Oncology Reports  
 DT Journal  
 LA English  
 CC 1-6 (Pharmacology)  
 AB The purpose of this study was to investigate and compare the effects of  
**paclitaxel** and its water-sol. conjugates (sodium-pentetic acid-  
**paclitaxel**; polyethylene glycol-**paclitaxel**, and  
 poly[L-glutamic acid]-**paclitaxel**) on chromosome morphol. and  
 induction of apoptosis in a metastatic murine melanoma cell line (K1735  
 clone X-21). For this, murine melanoma cells were treated continuously  
 for 72 h with three concns. (1.2 .mu.M, 2.4 .mu.M, and 4.8 .mu.M) of each  
 of **paclitaxel**, and conjugates. Another set of cells were  
 pulse-treated at 2.4 .mu.M, 4.8 .mu.M and 9.6 .mu.M concns. of each of  
 these drugs for 4 h and the recovered cells were examd. after 72 h.  
 Control cultures received only the solvents (DMSO or water). Our results  
 showed a significant increase in the frequencies of **telomeric**  
 assocns., chromosome aberrations, polyploidization, distorted and  
 disintegrated chromosome morphol., and reduced **telomeric** signal  
 intensity by fluorescence in situ hybridization, in treated cultures as  
 compared to the controls. However, we detected no change in  
**telomerase** activity. In addn., the majority of interphase nuclei  
 in treated cells showed apoptotic bodies, with chromatin condensation.  
 These in vitro results suggest that cell death induced by  
**paclitaxel** and its water-sol. conjugates is due to the loss of  
**telomeric** repeats, as shown by reduced signal fluorescence and  
 increased **telomeric** assocns.  
 ST melanoma metastasis **paclitaxel telomere**  
**telomerase**  
 IT Chromatin  
 Chromosome aberrations  
**Telomeres** (chromosome)  
 (cell-killing by **paclitaxel** in a metastatic murine melanoma  
 cell line is mediated by extensive **telomere** erosion with no  
 decrease in **telomerase** activity)  
 IT Antitumor agents  
 Antitumor agents  
 Antitumor agents  
 (melanoma, metastasis; cell-killing by **paclitaxel** in a  
 metastatic murine melanoma cell line is mediated by extensive  
**telomere** erosion with no decrease in **telomerase**  
 activity)  
 IT 33069-62-4, **Paclitaxel** 33069-62-4D,  
**Paclitaxel**, conjugates  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (cell-killing by **paclitaxel** in a metastatic murine melanoma  
 cell line is mediated by extensive **telomere** erosion with no  
 decrease in **telomerase** activity)  
 IT 120178-12-3, **Telomerase**  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (cell-killing by **paclitaxel** in a metastatic murine melanoma  
 cell line is mediated by extensive **telomere** erosion with no  
 decrease in **telomerase** activity)  
 RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
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- (24) Wiernik, P; J Clin Oncol 1987, V5, P1232 MEDLINE

IT 33069-62-4, Paclitaxel 33069-62-4D,

Paclitaxel, conjugates

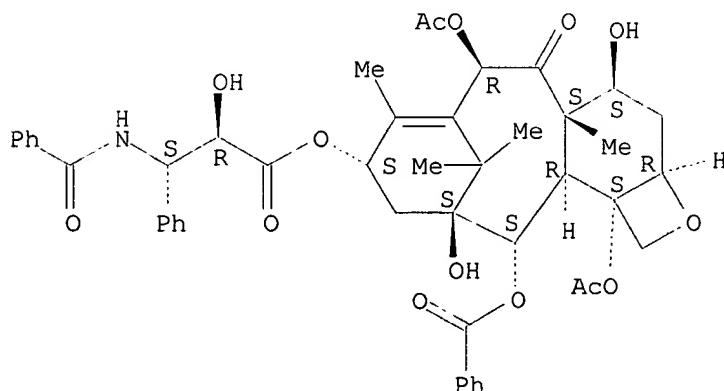
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cell-killing by paclitaxel in a metastatic murine melanoma cell line is mediated by extensive telomere erosion with no decrease in telomerase activity)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

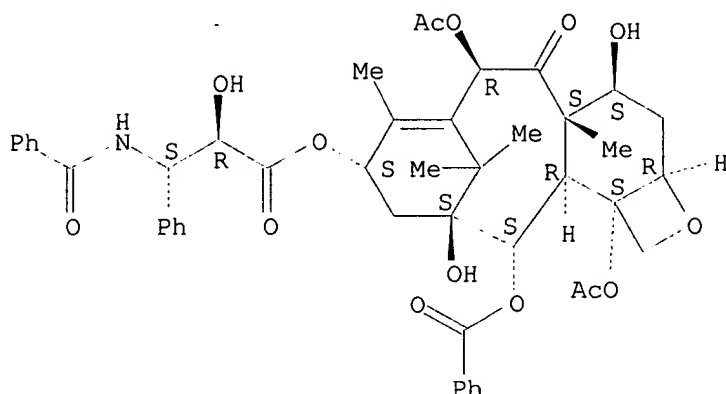
Absolute stereochemistry. Rotation (-).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 120178-12-3, **Telomerase**  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (cell-killing by **paclitaxel** in a metastatic murine melanoma  
 cell line is mediated by extensive **telomere** erosion with no  
 decrease in **telomerase** activity)  
 RN 120178-12-3 HCAPLUS  
 CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA  
 INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L65 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:764282 HCAPLUS

DN 130:20546

TI HIV and **cancer** treatment

IN Camden, James Berger

PA The Procter & Gamble Company, USA

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-41

ICS A61K031-415; A61K031-66

CC 1-5 (Pharmacology)

FAN.CNT 1

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE         |
|----|---------------|--|----------|-----------------|--------------|
| PI | WO 9851303    | A1   | 19981119 | WO 1997-US21564 | 19971126 <-- |
|    | W:            | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |              |
|    | RW:           | GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG   |          |                 |              |
|    | ZA 9709095    | A  | 19980511 | ZA 1997-9095    | 19971010 <-- |
|    | AU 9874029    | A1   | 19981208 | AU 1998-74029   | 19971126 <-- |
|    | EP 954309     | A1   | 19991110 | EP 1997-949599  | 19971126 <-- |
|    | R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI   |          |                 |              |
|    | BR 9712981    | A  | 20000418 | BR 1997-12981   | 19971126 <-- |
|    | CN 1254281    | A  | 20000524 | CN 1997-182189  | 19971126 <-- |
|    | JP 2000510156 | T2   | 20000808 | JP 1998-522997  | 19971126 <-- |
|    | NO 9901701    | A  | 20000117 | NO 1999-1701    | 19990409 <-- |



KR 2000049064      A      20000725      KR 1999-703137      19990410 <--  
PRAI US 1997-46726P      P      19970516 <--  
WO 1997-US21564      W      19971126 <--

AB A method of treating HIV or other viral infections by administering a herbicide or fungicide or deriv. thereof to an animal or human. The fungicides or herbicides can be used in conjunction with other treatments, e.g. with AZT or protease inhibitors for the treatment of HIV. For example, thiabendazole and chloropropham have been shown to quickly reduce the level of virus prodn. from cell populations chronically infected with HIV-1 and the antiviral effect is maintained with continued compd. exposure. This redn. of virus prodn. occurs at concns. which are non toxic to the host cell and which have no effect on the syntheses of cellular DNA, RNA and protein. Further, chronically infected cells treated for prolonged periods of time with thiabendazole and chloropropham were not super-infected with HIV. A method for inhibiting the growth of tumors and cancers in mammals comprising administering a herbicidal or fungicidal deriv. is also disclosed herein. The fungicides or herbicides can be used in conjunction with other treatments, e.g. taxol for the treatment of breast cancer. Potentiators can also be included in the herbicidal or fungicidal compn. This method is particularly effective when the cancer or virus is an animal cell genetically modified by plant or fungus genetic material. A chemotherapeutic agent can also be administered first to significantly reduce the size of the cancer and then the treatment with the herbicide or fungicide is used. These methods are particularly effective when the cancer or virus is a mutated cell comprising plant or fungal genetic material.

ST herbicide fungicide antitumor antiviral HIV

IT Intestine, neoplasm  
(colon, inhibitors; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Antitumor agents  
(colon; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Lung, neoplasm  
(inhibitors; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Antitumor agents  
(leukemia; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Drug delivery systems  
(liposomes; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Antitumor agents  
(lung; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Antitumor agents  
(mammary gland; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Antitumor agents  
(melanoma; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Mammary gland  
(neoplasm, inhibitors; therapy of cancer and viral infections with drugs in combination with fungicides and herbicides)

IT Antitumor agents  
Antiviral agents  
Fungicides  
Herbicides  
Human immunodeficiency virus 1  
(therapy of cancer and viral infections with drugs in

**combination** with fungicides and herbicides)

IT 144114-21-6, Retropepsin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; therapy of **cancer** and viral infections with  
 drugs in **combination** with fungicides and herbicides)

IT 50-18-0, Cyclophosphamide 50-44-2, 6-Mercaptopurine 50-76-0,  
 Dactinomycin 50-91-9 51-17-2, Benzimidazole 51-21-8, Fluorouracil  
 59-05-2, Methotrexate 101-21-3, Chloropropham 126-07-8, Griseofulvin  
 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-79-8 154-42-7,  
 6-Thioguanine 320-67-2, Azacytidine 645-05-6, Altretamine 768-94-5,  
 Amantadine 1071-83-6 9015-68-3, Asparaginase 10605-21-7  
 11056-06-7, Bleomycin 15663-27-1, Cisplatin 17804-35-2, Benomyl  
 18378-89-7, Plicamycin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin  
 25316-40-9, Adriamycin 29767-20-2, Teniposide 30516-87-1,  
 3'-Azido-3'-deoxythymidine 33069-62-4, Taxol  
 33419-42-0, Etoposide 34435-09-1, A-36683 53910-25-1, Pentostatin  
 60207-90-1, Propiconazole 76849-19-9, CB3717 86386-73-4, Fluconazole  
 125317-39-7, Navelbine 216252-30-1, Cyctrabine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (therapy of **cancer** and viral infections with drugs in  
**combination** with fungicides and herbicides)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

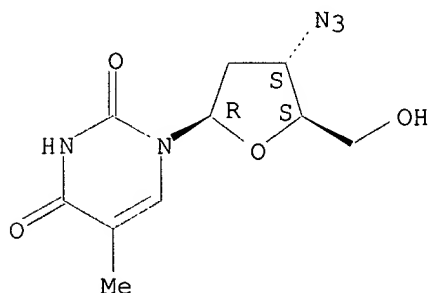
RE  
 (1) Merck & Co; EP 0617968 A 1994 HCAPLUS  
 (2) Procter & Gamble; WO 9632103 A 1996 HCAPLUS  
 (3) Procter & Gamble; WO 9632104 A 1996 HCAPLUS  
 (4) Procter & Gamble; WO 9632115 A 1996 HCAPLUS  
 (5) Procter & Gamble; WO 9705873 A 1997 HCAPLUS

IT 30516-87-1, 3'-Azido-3'-deoxythymidine 33069-62-4,  
 Taxol  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (therapy of **cancer** and viral infections with drugs in  
**combination** with fungicides and herbicides)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

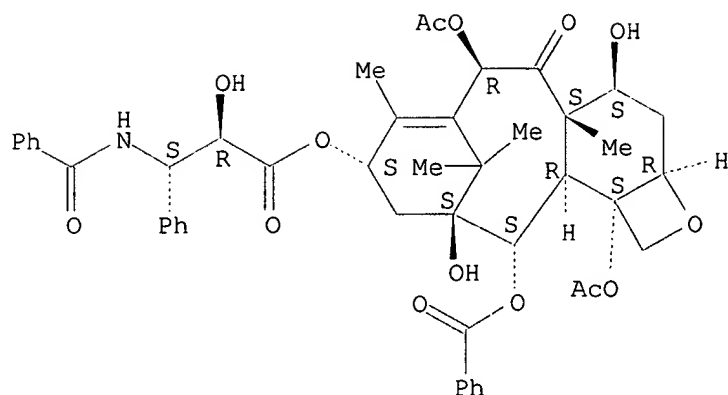
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,  
 (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-  
 tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl  
 ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:729760 HCAPLUS

DN 130:137432

TI Molecular and biological features of two new human squamous and adenocarcinoma of the lung cell lines

AU Gasperi-Campani, Anna; Roncuzzi, Laura; Ricotti, Luca; Lenzi, Laura; Gruppioni, Rita; Sensi, Alberto; Zini, Nicoletta; Zoli, Wainer; Amadori, Dino

CS Department of Experimental Pathology, University of Bologna, Bologna, 40126, Italy

SO Cancer Genetics and Cytogenetics (1998), 107(1), 11-20  
CODEN: CGCYDF; ISSN: 0165-4608

PB Elsevier Science Inc.

DT Journal

LA English

CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1, 3

AB Two human cancer cell lines were established from metastatic lesions of an adenocarcinoma (RAL) and a squamous cell (CAEP) carcinoma of the lung. The clin. histories of the patients from whom the cell lines were derived are reported. The lines were maintained in continuous culture with doubling times of 65 (RAL) and 50 (CAEP) hours. The RAL and CAEP cell lines, whose morphol. and ultrastructural features are presented, showed extensively rearranged karyotypes with modal no. of 85 (RAL) and 98 (CAEP). In particular, chromosome 2 pentasomy and several clonal markers were evident in the RAL cells, whereas a **telomeric** deletion of chromosome 1, del(1)(q32), was obsd. in the CAEP cells. The morphol. data were confirmed by high expression of specific antigens for each histotype. A marked positivity of the neuron-specific enolase (NSE) levels was evident by immunoenzymic assays in the cell lines cytosol with respect to those present in the resp. patient's sera. No amplification or rearrangements were evident in the CMYC, LMYC, NMYC, INT-2, ERBB2, HRAS, KRAS, MOS, HST-1 genes by Southern blotting anal. in each cell line. Point mutations in exon 1 of KRAS and in exon 7 of TP53 were evident by polymerase chain reaction (PCR)-DNA sequencing in the RAL cell line, whereas no alterations were present in the HRAS and RB genes. The four genes studied did not show point mutations in the CAEP cell line. The RAL cell line was resistant to all the drugs tested, whereas the CAEP cells were sensitive to vinblastine. These cell lines may represent useful exptl. models to investigate lung cancer biol. and anticancer drug response.

ST chromosome aberration lung squamous cell carcinoma adenocarcinoma line;  
tumor antigen lung squamous cell carcinoma adenocarcinoma line; drug  
resistance lung squamous cell carcinoma adenocarcinoma line

IT Keratins

- RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(17; mol. and biol. features of two new human squamous and  
adenocarcinoma of lung cell lines)
- IT Keratins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(19; mol. and biol. features of two new human squamous and  
adenocarcinoma of lung cell lines)
- IT Antigens  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(HPA (human pulmonary adenocarcinoma); mol. and biol. features of two  
new human squamous and adenocarcinoma of lung cell lines)
- IT Animal cell line  
(RAL and CAEP; mol. and biol. features of two new human squamous and  
adenocarcinoma of lung cell lines)
- IT Gene, animal  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP  
(Properties); BIOL (Biological study); OCCU (Occurrence)  
(TP53, mutation; mol. and biol. features of two new human squamous and  
adenocarcinoma of lung cell lines)
- IT Lung, neoplasm  
(adenocarcinoma, metastasis; mol. and biol. features of two new human  
squamous and adenocarcinoma of lung cell lines)
- IT Drug resistance  
(antitumor; drug resistance of two new human squamous and  
adenocarcinoma of lung cell lines)
- IT Gene, animal  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP  
(Properties); BIOL (Biological study); OCCU (Occurrence)  
(c-Ki-ras, mutation; mol. and biol. features of two new human squamous  
and adenocarcinoma of lung cell lines)
- IT Cytoplasm  
(cytosol, neuron-specific enolase in; mol. and biol. features of two  
new human squamous and adenocarcinoma of lung cell lines)
- IT Mutation  
(deletion, del(1)(q32); mol. and biol. features of two new human  
squamous and adenocarcinoma of lung cell lines)
- IT Keratins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(high-mol.-wt.; mol. and biol. features of two new human squamous and  
adenocarcinoma of lung cell lines)
- IT Chromosome  
(human 1, deletion del(1)(q32); mol. and biol. features of two new  
human squamous and adenocarcinoma of lung cell lines)
- IT Chromosome  
(human 2, pentasomy; mol. and biol. features of two new human squamous  
and adenocarcinoma of lung cell lines)
- IT Neoplasm  
(metastasis, from lung; mol. and biol. features of two new human  
squamous and adenocarcinoma of lung cell lines)
- IT Cell morphology  
Chromosome aberrations  
Disease models  
(mol. and biol. features of two new human squamous and adenocarcinoma  
of lung cell lines).
- IT Carcinoembryonic antigen  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(mol. and biol. features of two new human squamous and adenocarcinoma  
of lung cell lines)

- IT p53 (protein)  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
(mutation; mol. and biol. features of two new human squamous and adenocarcinoma of lung cell lines)
- IT Ras proteins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
(p21c-Ki-ras, mutation; mol. and biol. features of two new human squamous and adenocarcinoma of lung cell lines)
- IT Mutation  
(point; mol. and biol. features of two new human squamous and adenocarcinoma of lung cell lines)
- IT Antitumor agents  
(resistance to; drug resistance of two new human squamous and adenocarcinoma of lung cell lines)
- IT Lung, neoplasm  
(squamous cell carcinoma, metastasis; mol. and biol. features of two new human squamous and adenocarcinoma of lung cell lines)
- IT 50-07-7, Mitomycin-C 51-21-8 865-21-4, Vinblastine 3778-73-2, Ifosfamide 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 33069-62-4, Taxol 33419-42-0, Etoposide 39800-16-3, 4-Hydroperoxycyclophosphamide 41575-94-4, Carboplatin 71486-22-1, Vinorelbine 95058-81-4, Gemcitabine 114977-28-5, Taxotere  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drug resistance of two new human squamous and adenocarcinoma of lung cell lines)
- IT 9014-08-8, Enolase  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(neuron-specific; mol. and biol. features of two new human squamous and adenocarcinoma of lung cell lines)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

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IT 33069-62-4, Taxol

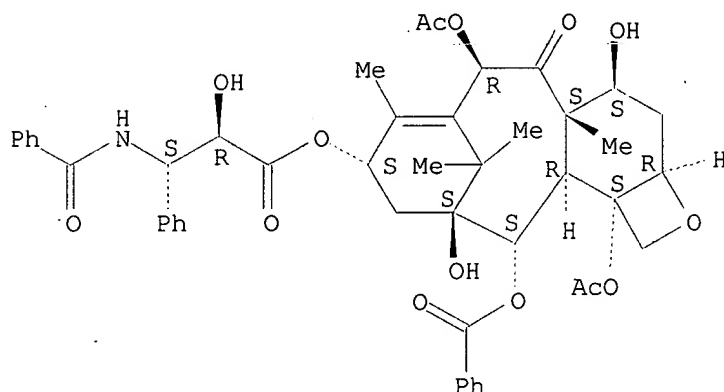
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug resistance of two new human squamous and adenocarcinoma of lung cell lines)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:562471 HCAPLUS

DN 129:311598

TI Cytogenetic and molecular characterization of random chromosomal rearrangements activating the drug resistance gene, MDR1/P-glycoprotein, in drug-selected cell lines and patients with drug refractory ALL

AU Knutsen, Turid; Mickley, Lyn A.; Ried, Thomas; Green, Eric D.; Du Manoir, Stanislas; Schrock, Evelin; Macville, Marryn; Ning, Yi; Robey, Robert; Polymeropoulos, Mihael; Torres, Rosarelis; Fojo, Tito

CS Medicine Branch, Division of Clinical Sciences, NCI, NIH, Bethesda, MD, USA

SO Genes, Chromosomes & Cancer (1998), 23(1), 44-54

CODEN: GCCAES; ISSN: 1045-2257

PB Wiley-Liss, Inc.

DT Journal

LA English

CC 3-4 (Biochemical Genetics)  
Section cross-reference(s): 1, 14

AB Drug resistance, both primary and acquired, is a major obstacle to advances in cancer chemotherapy. In vitro, multidrug resistance can be mediated by P-glycoprotein (PGY1), a cell surface phosphoglycoprotein that acts to efflux natural products from cells. PGY1 is encoded by the MDR1 gene located at 7q21.1. Overexpression of MDR1 has been demonstrated in many cancers, both in patient tumors and in cell lines selected with a variety of chemotherapeutic agents. Recent studies in drug-selected cell lines and patients samples have identified hybrid mRNAs comprised of an active, but apparently random, gene fused 5' to MDR1 by constitutively expressed genes may be a mechanism for activation of this gene following

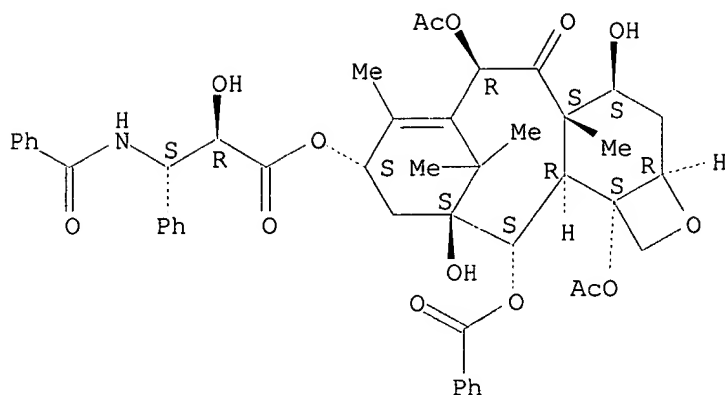
drug exposure. In this study, fluorescence in situ hybridization (FISH) using whole chromosome paints (WCP) and bacterial artificial chromosome (BAC)-derived probes showed structural rearrangements involving 7q in metaphase and interphase cells, and comparative genomic hybridization (CGH) revealed high levels of amplification at chromosomal breakpoints. In an adriamycin-selected resistant colon cancer line (S48-3s/Adr), WCP4/WCP7 revealed t(4;7)(q31;q21) and BAC-derived probes demonstrated that the breakpoint lay between MDR1 and sequences 500-1000 kb **telomeric** to it. Similarly, in a subline isolated following exposure to actinomycin D (S48-3s/ActD), a hybrid MDR1 gene composed of heme oxygenase-2 sequences (at 16p13) fused to MDR1 was identified and a rearrangement confirmed with WCP7 and a **subtelomeric** 16p probe. Likewise, in a **paclitaxel**-selected MCF-7 subline where CASP sequences (at 7q22) were shown to be fused to MDR1, WCP7 showed an elongated chromosome 7 with a homogeneously staining regions (hsr); BAC-derived probes demonstrated that the hsr was composed of highly amplified MDR1 and CASP sequences. In all three selected cell lines, CGH demonstrated amplification at breakpoints involving MDR1 (at 7q21) and genes fused to MDR1 at 4q31, 7q22, and 16p13.3. Finally, in samples obtained from two patients with drug refractory ALL, BAC-derived probes applied to archived marrow cells demonstrated that a breakpoint occurred between MDR1 and sequences 500-1000 kb **telomeric** to MDR1, consistent with a random chromosomal rearrangement. These results support the proposal that random chromosomal rearrangement leading to capture and activation of MDR1 is a mechanism of acquired drug resistance.

- ST chromosome rearrangement drug resistance gene activation; gene MDR1 activation drug resistance leukemia; P glycoprotein gene drug resistance leukemia
- IT Gene, animal  
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)  
 (CASP (CAAT displacement protein alternatively spliced product); chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Gene, animal  
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)  
 (HMOX2; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 and heme oxygenase 2 gene in drug resistance)
- IT Gene, animal  
 Multidrug resistance proteins  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (MDR1; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Gene, animal  
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)  
 (NRF1; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Glycoproteins, specific or class  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (P170; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Leukemia  
 (acute lymphocytic; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Mutation  
 (chromosomal rearrangements activating P-glycoprotein multidrug

- resistance gene MDR1 and heme oxygenase 2 gene in drug resistance)
- IT Drug resistance  
(chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Intestine, neoplasm  
(colon, adenocarcinoma; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected colon adenocarcinoma cell line)
- IT Chromosome  
(human 16; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Chromosome  
(human 1; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Chromosome  
(human 4; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Chromosome  
(human 7; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Nucleic acid hybridization  
(in situ, fluorescence; detection of chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT Recombination, genetic  
(rearrangement; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells and patients with drug refractory acute lymphoblastic leukemia)
- IT 9059-22-7, Heme oxygenase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(2; chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 and heme oxygenase 2 gene in drug resistance)
- IT 50-76-0, Actinomycin D 25316-40-9, Adriamycin **33069-62-4, Paclitaxel**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells)
- IT **33069-62-4, Paclitaxel**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chromosomal rearrangements activating P-glycoprotein multidrug resistance gene MDR1 in drug-selected cells)
- RN 33069-62-4 HCAPLUS
- CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).





L65 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:200650 HCAPLUS

DN 128:265840

TI **Paclitaxel** and water-soluble poly(L-glutamic acid)-

**paclitaxel** induce direct chromosomal abnormalities and cell death in a murine metastatic melanoma cell line

AU Multani, Asha S.; Li, Chun; Ozen, Mustafa; Yadav, Maneesha; Yu, Dong-Fang; Wallace, Sidney; Pathak, Sen

CS Department of Cell Biology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SO Anticancer Research (1997), 17(6D), 4269-4274  
CODEN: ANTRD4; ISSN: 0250-7005

RC261.A1.A68

PB Anticancer Research

DT Journal

LA English

CC 1-6 (Pharmacology)

AB The effects of **paclitaxel** and water-sol. poly(L-glutamic acid)-

**paclitaxel** (PG-TXL) on chromosome morphol., **telomeric** assocns., and induction of cell death were studied in a murine melanoma cell line (K-1735 clone X-21). Cells were treated with various concns. (0.1-8.0 .mu.g/mL) of **paclitaxel** alone, PG alone, or PG-TXL for 2 h and 4 h and harvested immediately without recovery. The frequency of metaphases with **telomeric** assocns. increased, metaphases had clumped and distorted chromosome morphol., cells accumulated in metaphase (mitotic arrest), and cell death had been induced. Cells treated with PG-TXL showed more such abnormalities than did cells treated with either **paclitaxel** or PG alone. PG-TXL may be superior to **paclitaxel** alone in inducing cytotoxic effects, and these effects could be mediated by various chromosomal abnormalities in cancer cells.

ST **paclitaxel** polyglutamate conjugate melanoma chromosome mitosis; antitumor **paclitaxel** polyglutamate conjugate

IT Antitumor agents

(melanoma; chromosomal abnormalities and cell death induction by **paclitaxel** and **paclitaxel**-poly(L-glutamate) conjugate as)

IT Antitumor agents

(metastasis; chromosomal abnormalities and cell death induction by **paclitaxel** and **paclitaxel**-poly(L-glutamate) conjugate as)

IT Chromosome

(**paclitaxel** and **paclitaxel**-poly(L-glutamate) conjugate induction of chromosomal abnormalities in metastatic melanoma cells)

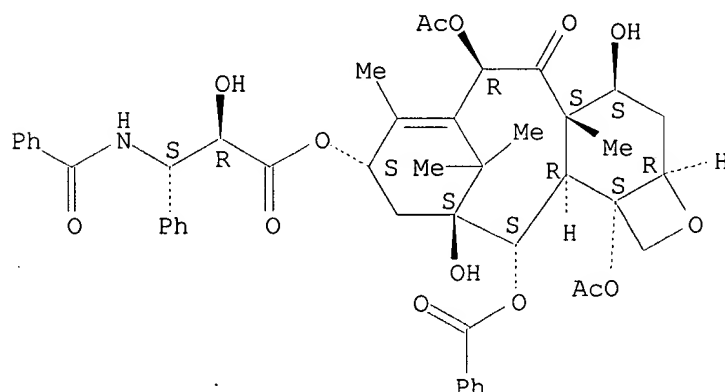
IT Mitosis

(**paclitaxel** and **paclitaxel**-poly(L-glutamate))

conjugate induction of mitotic abnormalities in metastatic melanoma cells)

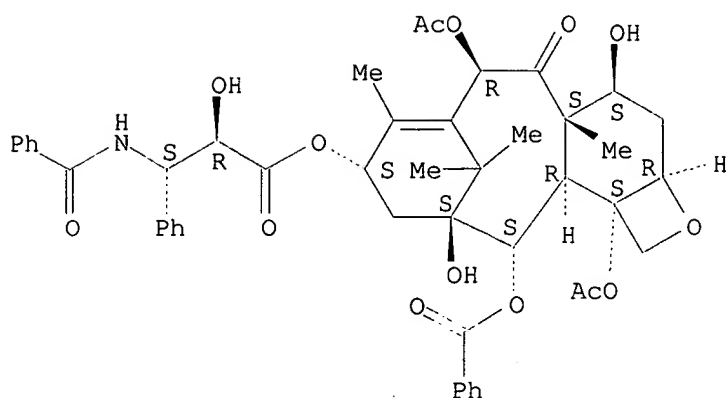
- IT 25513-46-6D, Poly(L-glutamic acid), conjugate with **paclitaxel**  
**33069-62-4, Paclitaxel 33069-62-4D,**  
**Paclitaxel**, conjugate with poly(L-glutamic acid)  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (chromosomal abnormalities and cell death in metastatic melanoma cells induction by)
- IT **33069-62-4, Paclitaxel 33069-62-4D,**  
**Paclitaxel**, conjugate with poly(L-glutamic acid)  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (chromosomal abnormalities and cell death in metastatic melanoma cells induction by)
- RN 33069-62-4 HCAPLUS
- CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



- RN 33069-62-4 HCAPLUS
- CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L65 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:29884 HCAPLUS

DN 128:178752

TI Inhibition of **telomerase** activity by PKC inhibitors in human nasopharyngeal cancer cells in culture

AU Ku, Wei-Chi; Cheng, Ann-Joy; Wang, Tzu-Chien V.

CS Department of Molecular and Cellular Biology, College of Medicine, Chang Gung University, Kwei-San, Taiwan

SO Biochemical and Biophysical Research Communications (1997), 241(3), 730-736

CODEN: BBRCA9; ISSN: 0006-291X

PB Academic Press

DT Journal

LA English

CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1, 7, 13

AB **Telomerase** is a specialized ribonucleoprotein polymerase that adds hexanucleotides (TTAGGG) onto human chromosomal ends. The expression of **telomerase** activity has been assocd. with cell immortalization and the malignant phenotype in most cancers. How the **telomerase** activity is regulated in cancer cells is presently not known. In this work, the effects of cell cycle blockers, DNA damaging agents, TopII inhibitors and proteins kinase inhibitors on the **telomerase** activity were examd. in cultured nasopharyngeal carcinoma cells NPC-076. Agents which interfere with tubulin assembly (Taxol and vinblastine) and agents which arrest cells at S phase (methotrexate and 5-fluorouracil) did not inhibit **telomerase** activity of treated cells. Agents which damage DNA (cisplatin, Me methanesulfonate, and UV radiation) and TopII inhibitors (etoposide and daunorubicin) also did not inhibit **telomerase** activity of treated cells. Among the protein kinase inhibitors examd., no significant inhibition of **telomerase** activity was obsd. with cells treated with quercetin, H-89, or herbimycin A. On the other hand, two protein kinase C (PKC) inhibitors (bisindolylmaleimide I and H-7) were found to produce a big inhibition of **telomerase** activity in treated cells. Staurosporine produced a moderate inhibition, and sphingosine had a small inhibitory effect. The inhibition of **telomerase** activity by PKC inhibitors appears to be specific since the treated cells were mostly viable (i.e., greater than 75%) and still retained significant levels of protein synthesis capability. These results implicate that protein kinase C is involved in the regulation of **telomerase** activity in vivo.

ST **telomerase** regulation protein kinase C cancer; antitumor PKC inhibitor **telomerase**

IT Antitumor agents

## Neoplasm

(inhibition of **telomerase** activity by PKC inhibitors in human nasopharyngeal cancer cells)

- IT 62996-74-1, Staurosporine 84477-87-2, H-7 169939-94-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibition of **telomerase** activity by PKC inhibitors in human nasopharyngeal cancer cells)
- IT 120178-12-3, **Telomerase** 141436-78-4, Protein kinase C  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibition of **telomerase** activity by PKC inhibitors in human nasopharyngeal cancer cells)
- IT 120178-12-3, **Telomerase**  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibition of **telomerase** activity by PKC inhibitors in human nasopharyngeal cancer cells)
- RN 120178-12-3 HCAPLUS
- CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

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L103 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2002:386690 BIOSIS

DN PREV200200386690

TI Simultaneous targeting of telomeres and telomerase as a cancer therapeutic approach.

AU Mo, Yiqun (1); Gan, Yuebo (1); Johnston, Jeffrey S. (1); Song, Saehum (1); Xiao, Xiaodong (1); **Wientjes, M. Guillaume (1); Au, Jessie L.-S. (1)**

CS (1) Ohio State University, Columbus, OH USA

SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 251. print.

Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002

ISSN: 0197-016X.

DT Conference

LA English

CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals \*00520

Cytology and Cytochemistry - Human \*02508

Biochemical Studies - General \*10060

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines \*10062

Enzymes - General and Comparative Studies; Coenzymes \*10802

Pathology, General and Miscellaneous - Therapy \*12512

Pharmacology - General \*22002

Pharmacology - Clinical Pharmacology \*22005  
 Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects \*24004  
 Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy \*24008  
 BC Hominidae 86215  
 IT Major Concepts  
     Pharmacology; Tumor Biology  
 IT Parts, Structures, & Systems of Organisms  
     telomere  
 IT Chemicals & Biochemicals  
     3'-azido-3'-deoxythymidine [AZT]: antineoplastic - drug,  
     enzyme inhibitor - drug; RNA; **paclitaxel**: antineoplastic -  
     drug; telomerase: regulation  
 IT Miscellaneous Descriptors  
     cell growth rate; Meeting Abstract  
 ORGN Super Taxa  
     Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia  
 ORGN Organism Name  
     FaDu cell line (Hominidae): apoptosis, human pharynx tumor cells  
 ORGN Organism Superterms  
     Animals; Chordates; Humans; Mammals; Primates; Vertebrates  
 RN 30516-87-1 (3'-AZIDO-3'-DEOXYTHYMIDINE)  
     33069-62-4 (**PACLITAXEL**)  
     120178-12-3 (TELOMERASE)

L103 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 2001:468784 BIOSIS  
 DN PREV200100468784  
 TI 3'-azido3'-deoxythymidine enhances **paclitaxel** activity in human  
     FaDu cells.  
 AU Johnston, Jeffrey S. (1); Wientjes, M. Guillaume (1); Au,  
     **Jessie L.-S.** (1)  
 CS (1) The Ohio State University, Columbus, OH USA  
 SO Proceedings of the American Association for Cancer Research Annual  
     Meeting, (March, 2001) Vol. 42, pp. 507. print.  
     Meeting Info.: 92nd Annual Meeting of the American Association for Cancer  
     Research New Orleans, LA, USA March 24-28, 2001  
     ISSN: 0197-016X.  
 DT Conference  
 LA English  
 SL English  
 CC General Biology - Symposia, Transactions and Proceedings of Conferences,  
     Congresses, Review Annuals \*00520  
     Cytology and Cytochemistry - Human \*02508  
     Biochemical Studies - General \*10060  
     Biochemical Studies - Nucleic Acids, Purines and Pyrimidines \*10062  
     Pathology, General and Miscellaneous - Therapy \*12512  
     Pharmacology - General \*22002  
     Pharmacology - Clinical Pharmacology \*22005  
     Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic  
     Effects \*24004  
 BC Hominidae 86215  
 IT Major Concepts  
     Pharmacology; Tumor Biology  
 IT Chemicals & Biochemicals  
     3'-azido-3'-deoxythymidine [AZT]: antineoplastic - drug,  
     pharmaceutical adjunct - drug; **paclitaxel**: AZT  
     -induced antitumor activity enhancement, antineoplastic - drug  
 IT Miscellaneous Descriptors  
     drug regimen; Meeting Abstract  
 ORGN Super Taxa  
     Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia  
 ORGN Organism Name

FaDu cell line (Hominidae): combination drug treatment, human epidermoid carcinoma cell line, in-vitro model system

ORGN Organism Superterms  
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 30516-87-1 (3'-AZIDO-3'-DEOXYTHYMIDINE)  
33069-62-4 (PACLITAXEL)

L103 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:369554 BIOSIS

DN PREV200100369554

TI AZT enhances antitumor activity of paclitaxel in human FaDu xenografts in mice.

AU Song, SaeHeum (1); Wientjes, M. Guill (1); Au, Jessie L.-S. (1)

CS (1) Ohio State University, Columbus, OH USA

SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 81. print.  
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001  
ISSN: 0197-016X.

DT Conference

LA English

SL English

CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals \*00520  
Cytology and Cytochemistry - Animal \*02506  
Cytology and Cytochemistry - Human \*02508  
Biochemical Studies - General \*10060  
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines \*10062  
Pathology, General and Miscellaneous - Therapy \*12512  
Pharmacology - General \*22002  
Pharmacology - Clinical Pharmacology \*22005  
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects \*24004  
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy \*24008  
Chemotherapy - Antiviral Agents \*38506

BC Hominidae 86215  
Muridae 86375

IT Major Concepts  
Infection; Pharmacology; Tumor Biology

IT Chemicals & Biochemicals  
3-'azidothymidine [AZT]: antiviral - drug,  
paclitaxel activity enhancer; paclitaxel:  
antineoplastic - drug

IT Miscellaneous Descriptors  
apoptosis; body weight loss; drug interactions; Meeting Abstract

ORGN Super Taxa  
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
FaDu cell line (Hominidae): human pharynx tumor cells; mouse (Muridae): animal model

ORGN Organism Superterms  
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

RN 30516-87-1 (3-'AZIDOTHYMIDINE)  
33069-62-4 (PACLITAXEL)

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FILE 'WPIX' ENTERED AT 12:38:04 ON 15 DEC 2002  
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 MOST RECENT DERWENT UPDATE: 200280 <200280/DW>  
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[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

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[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

=> d 1124 all abeq tech abex tot

L124 ANSWER 1 OF 3 WPIX (C) 2002 THOMSON DERWENT

AN 2001-071022 [08] WPIX

DNC C2001-019846

TI Inhibiting or reducing growth of cell for treating cancer, comprising administering telomere damage-inducing agent and telomerase inhibitory agent to the cell.

DC B04 B05 D16

IN AU, J L; WIENTJES, G

PA (AUJL-I) AU J L; (WIEN-I) WIENTJES G

CYC 92

PI WO 2000074667 A2 20001214 (200108)\* EN 97p A61K031-00

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
 LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG  
 SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000054665 A 20001228 (200119) A61K031-00

ADT WO 2000074667 A2 WO 2000-US15544 20000605; AU 2000054665 A AU 2000-54665 20000605

FDT AU 2000054665 A Based on WO 200074667

PRAI US 1999-137549P 19990604

IC ICM A61K031-00

AB WO 200074667 A UPAB: 20010207

NOVELTY - Inhibiting or reducing the growth of a cell (M1), comprising administering a telomere damage-inducing agent (I) and a telomerase inhibitory agent (II) to the cell, so that an inhibition or reduction in the growth of the cell is achieved, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) identifying (M2) an agent or agents that inhibits or reduces the growth of a cell, comprising:

- (a) contacting a cell with at least one agent;
- (b) determining if telomere damage has occurred;
- (c) contacting a cell with the same or another agent; and
- (d) determining if a reduction in telomerase activity has occurred,

where an agent or agents, alone or in combination, that are determined to induce telomere damage and inhibit telomerase activity, are inhibits of cell growth;

- (2) an agent or agents identified by (M2);

- (3) a pharmaceutical composition (III) comprising the agent or agents identified by (M2);
- (4) a composition (IV) suitable for inhibiting or reducing the growth of a cell comprising (I) and (II);
- (5) an article (V) of manufacture comprising a vial containing (I) and (II) which are purified;
- (6) enhancing (M3) the efficacy of a chemotherapeutic agent, comprising administering a chemotherapeutic agent to a cell in the presence of (II);
- (7) detecting (M4) telomerase activity in cell extract, comprising:
  - (a) incubating a reaction mixture comprising a cell extract, a nucleic acid substrate for a telomerase, and nucleotide triphosphates, for the nucleic acid substrate to be polymerized,
  - (b) contacting the substrate with at least one nucleic acid primer and subjecting the substrate to a polymerase chain reaction; and
  - (c) detecting the presence of polymerase chain reaction products to detect telomerase activity in the cell extract;
- (8) determining (M5) telomere length, comprising:
  - (a) hybridizing telomeric DNA fragments with a telomere probe; and
  - (b) determining the amount of hybridized telomere probe present,where the amount of hybridized telomere probe present is an indication of telomere length; and
- (9) identifying (II), comprising:
  - (a) contacting a cell with an agent;
  - (b) incubating a reaction mixture comprising an extract of the cell, a nucleic acid substrate for a telomerase, and nucleotide triphosphates for the nucleic acid substrate to be polymerized,
  - (c) contacting the substrate with at least one nucleic acid primer;
  - (d) subjecting the substrate to a polymerase chain reaction; and
  - (e) detecting a decrease in the presence of polymerase chain reaction products to identify (II).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inhibitor of cell growth; inducer of telomere damage.

Antitumor effect of an agent that damages telomeres (i.e. **paclitaxel**) by the telomerase inhibitor **AZT**, in immunodeficient mice bearing human head and neck cancer FaDu xenografts, was tested. The activity of **paclitaxel**, with or without **AZT**, was evaluated in immunodeficient mice (male Balb/c nu/nu mice) bearing the human pharynx FaDu xenografts. The mice were divided into four treatment groups: saline control, **AZT**, **paclitaxel**, **paclitaxel**+**AZT**. The antitumor effect of the drug treatments was measured. The results showed that **AZT** enhanced the in vivo antitumor effect of **paclitaxel**, treatment with the combination of **paclitaxel** and **AZT** resulted in a decrease in tumor size, and animals in the control group, **paclitaxel** group, and **AZT** group showed an up to 4-fold increase in tumor size. The tumor size of the animals which received the combination of **paclitaxel** and **AZT** was significantly smaller than all other dose groups. Treatment with single agents (either **paclitaxel** or **AZT**) produced minimal toxicity with no toxicity-related death and minimal body weight loss compared to the pretreatment weight and the addition of **AZT** to **paclitaxel** did not enhance the body weight loss, indicating that **AZT** did not enhance the host toxicity of **paclitaxel**.

USE - The agent or agents identified by (M2) are useful for inhibiting or reducing the growth of a cell and for treating aberrant cell growth in a mammal, especially a human. (I) and (II) are useful for treating cancer, and identifying a patient having a cancer. (II) is useful for inhibiting or reducing resistance of a cell to (I). (All claimed). (I) and (II) are useful in screening assays for diagnosis, prognosis and treatment of cancer and in the design, formulation, synthesis, manufacture, and/or production of a drug or pharmaceutical composition for



use in the diagnosis, prognosis and treatment of cancer.

ADVANTAGE - The methods of measuring telomerase activity have increased sensitivity compared to prior art methods.

Dwg.0/10

FS CPI

FA AB; DCN

MC CPI: B04-B03B; B04-E01; B04-E05; B04-E06; B04-N04; B11-C08E1; B11-C08E3; B11-C08E5; B12-K04A1; B12-K04E; B12-K04F; B14-H01; B14-H01B; D05-H09; D05-H18B

TECH UPTX: 20010207

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M1) the growth is aberrant and the cell is a tumor cell of brain, breast, ovary, testes, bladder, prostate, colon, lung, liver, pancreas or uterus or the cell is a leukemic cell. The tumor is benign or malignant and the growth is hyperplastic or hypertrophic. The inhibition or reduction in the growth of the cell, preferably a human cell, comprises apoptosis. (I) is **paclitaxel** or its derivative and (II) is a nucleotide analog, such as **AZT** or **d4T** or its derivative or an antisense nucleic acid corresponding to a telomerase. In (M4), the cell extract is derived from a human cell that has been contacted with (II). (M4) further comprises contacting the cell extract with (II). The nucleic acid substrate comprises a sequence TTAGGG and the nucleic acid primer is labeled with a radioisotope or a fluorescent label and comprises sequences AATCCGTCGAGCAGAGTT and CCCTTACCCTTACCCTTACCCTTA. In (M5), the telomeric DNA fragments are produced using a restriction enzyme such as HinfI, HaeIII or HhaI and the telomeric DNA is derived from a cell that has been contacted with (II). The telomere probe comprises a sequence TTAGG and TTAGGGTTAGGGTTAGGGTTAGGG and is labeled with a radioisotope or a fluorescent label.

Preferred Formulation: (I) or (II) is formulated as a nanoparticle 500 nm-1 micro-m in diameter and comprises a cross linked gelatin or is formulated as a microparticle of about 1-10 micro-m diameter.

Preferred Agent: In (V), (I) and (II) are packaged in separate vials and are formulated in a carrier.

ABEX

ADMINISTRATION - (I) and (II) are administered locally, systemically, or regionally as a timed-release formulation and as a sub-therapeutic dose (claimed) at a dose of 0.0001-100, preferably 0.10-4 mg/kg. (IV) is administered by oral, nasal, parenteral, topical, rectal, vaginal, intralesional, intraorbital, intracapsular, intracisternal or ophthalmic route or by inhalation.

L124 ANSWER 2 OF 3 WPIX (C) 2002 THOMSON DERWENT

AN 2000-116702 [10] WPIX

DNC C2000-035674

TI Treatment of AIDS-associated Kaposi's sarcoma.

DC B02

IN DUCHIN, K; GRIFFING, S; HARRIMAN, G R; METTINGER, K L; DUCHIN, K L

PA (BAKE-N) BAKER NORTON PHARM INC

CYC 81

PI WO 9965307 A1 19991223 (200010)\* EN 41p A01N043-20

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA  
PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG  
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG  
UZ VN YU ZW

AU 9867873 A 20000105 (200024) A01N043-20

NO 9904712 A 19991126 (200026) A61K031-33

CN 1255041 A 20000531 (200045) A01N043-20

EP 1071329 A1 20010131 (200108) EN A01N043-20

R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2001114685 A 20010424 (200140)# 62p A61K031-337

KR 2001005949 A 20010115 (200151)# A61K031-36  
 JP 2002518297 W 20020625 (200243) 41p A61K031-337  
 ADT WO 9965307 A1 WO 1998-US6221 19980330; AU 9867873 A AU 1998-67873  
 19980330, WO 1998-US6221 19980330; NO 9904712 A WO 1998-US6221 19980327,  
 NO 1999-4712 19990927; CN 1255041 A CN 1998-805000 19980330, WO  
 1998-US6221 19980330; EP 1071329 A1 EP 1998-913281 19980330, WO  
 1998-US6221 19980330; JP 2001114685 A JP 1999-324494 19991008; KR  
 2001005949 A KR 1999-709026 19990927; JP 2002518297 W WO 1998-US6221  
 19980330, JP 2000-554198 19980330  
 FDT AU 9867873 A Based on WO 9965307; EP 1071329 A1 Based on WO 9965307; JP  
 2002518297 W Based on WO 9965307  
 PRAI WO 1998-US6221 19980330; US 1997-41651P 19970327; JP 1999-324494  
 19991008; KR 1999-709026 19990927  
 IC ICM A01N043-20; A61K031-33; A61K031-337; A61K031-36  
 ICS A61K045-00; A61P035-00; A61P037-04; A61P043-00  
 AB WO 9965307 A UPAB: 20010809  
 NOVELTY - Treatment of AIDS associated Kaposi's sarcoma comprises  
 concomitantly administering a taxane with one or more protease inhibitors.  
 ACTIVITY - Cytostatic; Anti-HIV. Initial treatment of AIDS-associated  
 Kaposi's sarcoma consisted of a 3 hour infusion of **paclitaxel** at  
 100 mg/m2 administered every 14 days, followed by treatment at 75 mg/m2.  
 The patient was a 33 year old black male diagnosed as HIV-positive in 1994  
 and suffering from Kaposi's sarcoma since February 1995. Previous  
 chemotherapy included DaunoXome (RTM) to which he showed stable disease  
 but had toxicity, and Adriamycin (RTM), bleomycin and vincristine, to  
 which he responded partially, but subsequently failed. The patient was on  
 antiretroviral therapy at the time he entered the protocol which consisted  
 of the protease inhibitor indinavir and two reverse transcriptase  
 inhibitors, **stavudine** and lamivudine. He continued on these  
 medications. During the treatment with the reduced dose of  
**paclitaxel**, after the first cycle, the patient showed a partial  
 response to **paclitaxel**. The Karnofsky performance score improved  
 from 60 at baseline to 90 at cycle 10 and the Symptom Distress Scale score  
 improved from 35 at baseline to 18 at cycle 10. A marked decrease in edema  
 and the prominence of facial lesions was seen by cycle 7.  
 MECHANISM OF ACTION - Protease-Inhibitor; Reverse-Transcriptase-  
 Inhibitor.  
 USE - The method can be used when treatment with liposomal  
 anthracyclines, liposomal doxorubicin, combinations of adriamycin,  
 bleomycin or vincristine, liposomal anthracyclines and combinations of  
 adriamycin, bleomycin or vincristine or two or more cytotoxic  
 chemotherapies have failed.  
 ADVANTAGE - The compositions are easily administered and can be given  
 at dosages that are safe and provide for manageable side effects.  
 Dwg.0/0  
 FS CPI  
 FA AB; DCN  
 MC CPI: B06-A03; B14-A02; B14-D06; B14-D07C; B14-G01B; **B14-H01**  
 TECH UPTX: 20000228  
 TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method - The method further  
 comprises concomitantly administering one or more reverse transcriptase  
 inhibitor.  
 ABEX  
 ADMINISTRATION - The dose of taxane is 30-200 (preferably 50-155,  
 especially 100) mg/m2 every two weeks. Preferably an induction therapy of  
 10 weeks is carried out.  
 L124 ANSWER 3 OF 3 WPIX (C) 2002 THOMSON DERWENT  
 AN 2000-022942 [02] WPIX  
 DNC C2000-005511  
 TI Composition for the treatment of cancer or infectious disease.  
 DC B04 B05 D16  
 IN BARTHOLEYNS, J; FOURON, Y; ROMET-LEMONNE, J

PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES  
 CYC 87  
 PI WO 9951248 A1 19991014 (200002)\* EN 26p A61K035-14  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ UG ZW  
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB  
 GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU  
 LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
 TT UA UG US UZ VN YU ZA ZW  
 AU 9931479 A 19991025 (200011) A61K035-14  
 EP 1067944 A1 20010117 (200105) EN A61K035-14  
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 JP 2002510639 W 20020409 (200227) 27p A61K035-14  
 ADT WO 9951248 A1 WO 1999-EP2105 19990329; AU 9931479 A AU 1999-31479  
 19990329; EP 1067944 A1 EP 1999-913310 19990329, WO 1999-EP2105 19990329;  
 JP 2002510639 W WO 1999-EP2105 19990329, JP 2000-542019 19990329  
 FDT AU 9931479 A Based on WO 9951248; EP 1067944 A1 Based on WO 9951248; JP  
 2002510639 W Based on WO 9951248  
 PRAI EP 1998-400783 19980402  
 IC ICM A61K035-14  
 ICS A61K045-00; A61P031-00; A61P035-00; C12N005-00; C12N005-08  
 ICI A61K031:00, A61K035:14, A61K038:19, A61K039:00; A61K031:00, A61K035-14;  
 A61K035-14, A61K038:19; A61K035-14, A61K039:00  
 AB WO 9951248 A UPAB: 20000112  
 NOVELTY - Combined composition contains the following individual  
 components, in the form of a kit-of-parts:  
 (a) monocyte derived cells, particularly cytotoxic macrophages; and  
 (b) chemotherapy or immunotherapy drugs, for the simultaneous,  
 separate or sequential use, for the treatment of cancer or infectious  
 diseases.  
 USE - The composition is useful for the treatment of cancer or  
 infectious diseases.  
 Dwg.0/2  
 FS CPI  
 FA AB; DCN  
 MC CPI: B02-A; B02-C; B02-P; B04-A07A; B04-F04; B04-H02B; B04-H02N; B04-H04;  
 B04-H05C; B04-M01; B05-A03B; B10-A07; B10-A13D; **B14-H01**;  
 D05-H07; D05-H08  
 TECH UPTX: 20000112  
 TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: The monocyte  
 derived cells contain chemotherapy or immunotherapy drugs. The  
 chemotherapy drug is selected among cytotoxic compounds such as  
 anthracyclins, daunorubicin, adriamycin, taxoter derivatives, vinca  
 alkaloids, vincristine, **taxol**, carmustine, cisplatin,  
 fluorouracils, cytostatic compounds such as polyamine inhibitors,  
 topoisomerase inhibitors, tamoxifen, prodasone, or sandostatin, or  
 compounds inducing apoptosis such as sodium butyrate or mitomycin C,  
 antibiotics such as penicillins, P-lactamines, cephalosporins, cyclins,  
 aminoglucosides, macrolides or sulfamides, or antiviral drugs such as  
**AZT**, protease inhibitors or acyclovir, **retrovir** or  
 foscarnet. The immunotherapy drug is selected from cytokines such as  
 cyclosporin, azathioprine, cyclophosphamide, IFN-gamma, IL-12, IL-2,  
 GM-CSF, G-CSF, immuno-adjuvants such as murapeptides or BCG, and vaccines  
 directed against tumor or infectious antigens, in the presence or not of  
 adjuvants.  
 Preparation: The monocyte derived cells are such as prepared by:  
 (i) recovery of blood derived mononuclear cells directly from blood  
 apheresis or from blood bag collection, followed if necessary by  
 centrifugation, to eliminate a substantial part of red blood cells  
 granulocytes and platelets, and collection of peripheral blood leukocytes;  
 (ii) washing peripheral blood leukocytes by centrifugation (to remove 90%  
 of platelets, red blood cells and debris) to obtain mononuclear cells;  
 (iii) resuspension of the total mononuclear cells (monocytes +

lymphocytes) obtained at the preceding step in culture medium (RPMI or IMDM type) at 10<sup>6</sup> to 2.10<sup>7</sup> cells/ml, possibly completed by cytokines and/or autologous serum, and culture for 5-10 days at 37 degreesC under O<sub>2</sub>/CO<sub>2</sub> atmosphere in hydrophobic gas permeable bags, to obtain monocyte derived cells and contaminating lymphocytes.

The process comprises the additional step of freezing at temperature below or equal to -80 degreesC aliquots of the above said suspension, with the addition of a cryo-preserved. The process comprises the additional step of melting said above frozen aliquots at a temperature enabling to obtain a suspension of monocyte derived cells, for instance at 4 degreesC, washing said suspension and resuspending it, for instance in an isotonic medium, to obtain a suspension of monocyte derived cells.

#### ABEX

ADMINISTRATION - The monocyte-derived cells and the chemotherapy or immunotherapy drugs are in the form of injectable solutions. The injectable solutions are in the form of locally injectable solutions. The injectable solutions are in the form of systemically injectable solutions. The monocyte derived cells are administered at a dose of 10<sup>7</sup>-10<sup>10</sup> (especially 10<sup>8</sup>-10<sup>9</sup>) monocyte derived cells per injection. The monocyte derived cells are administered in a repeated way up to ten times, the interval between each administration being between three days to two months. The immunotherapy or chemotherapy drug is administered at a dose of 0.1-1000 mg/day. In the case of administration of a drug chosen among immunotherapy drug, antiviral drug, cytotoxic drugs, or antibiotics, the drug being administered at a dose of 10-1000 mg/day. In the case of administration of a drug chosen among cytotoxic compounds, cytostatic compounds, compounds inducing apoptosis or cytokines, the drug is administered at a dose of 0.1-100 mg/day. The immunotherapy or chemotherapy drug is administered in a repeated way up to 10 times, the interval between each administration being between one day to two months. The chemotherapy or immunotherapy drug and the monocyte derived cells are injected simultaneously. The chemotherapy or immunotherapy drug and the monocyte-derived cells are administered in sequential way, the immunotherapy or chemotherapy drug being administered before the monocyte derived cells. The interval of time between the administration of the monocyte-derived cells and the administration of the immunotherapy or chemotherapy drugs is of one day to two months. The monocyte-derived cells and the chemotherapy or immunotherapy drug are administered sequentially, the monocytes derived cells being administered before the immunotherapy or chemotherapy drug. The monocyte-derived cells are administered before the administration of a vaccine directed to tumor or infectious antigens, the monocyte derived cells administration being possibly preceded by a chemotherapy treatment.

EXAMPLE - Patients, whose primary melanoma tumor was removed by surgery, are treated with chemotherapy agent (DTIC) (dacarbazine) after relapse. When their blood count is back to normal, blood is drawn up through apheresis in order to prepare large amounts of MD-APCS. These cells are then incubated for 4 hours with allogeneic tumor extract. 3 weekly subcutaneous injections (at 4 different sites) of 10<sup>7</sup> cells are made. Two months later, a cocktail of three antigens (MAGE-3, MELAN A and gp-100) plus adjuvant is injected to the patients in order to boost the immune system. The increased immune response is monitored by measuring the number of antigen specific CD8 T lymphocytes by ELISPOT technique. It is also assessed that the relapse-free time is significantly increased.

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(FILE 'REGISTRY' ENTERED AT 12:07:57 ON 15 DEC 2002)

FILE 'HCAPLUS' ENTERED AT 12:09:09 ON 15 DEC 2002

FILE 'MEDLINE' ENTERED AT 12:09:25 ON 15 DEC 2002

L66 7297 S L18  
 L67 9591 S L19 OR L20  
 L68 9591 S L66,L67  
 L69 6581 S L16  
 L70 8397 S L23  
 L71 8397 S L69,L70  
 L72 5 S L68 AND L71  
     E ANTISENSE/CT  
     E E6+ALL  
 L73 11150 S E17+NT  
     E NUCLEOTIDE/CT  
     E E48+ALL  
 L74 320607 S E7+NT  
 L75 965380 S D13./CT  
 L76 1168 S L71 AND L73-L75  
 L77 542 S (L73 OR L74 OR L75) (L) (TU OR AD OR PD)/CT AND L76  
 L78 436 S L77 AND C4./CT  
 L79 153 S L78 AND PY<=1999  
     E ANTINEOPLASTIC COMBINED CHEMOTHERAPY/CT  
     E E4+ALL  
 L80 47689 S E38+NT  
     E DRUG COMBINATION/CT  
     E E6+ALL  
 L81 34504 S E4  
     E DRUG THERAPY, COMBINATION/CT  
     E E3+ALL  
 L82 70827 S E4+NT  
 L83 319 S L77 AND L80-L82  
 L84 97 S L83 AND PY<=1999  
 L85 93 S L84 AND C4./CT  
 L86 83 S L85/ENG  
 L87 0 S L84 AND ?TELOMER?  
 L88 76 S L86 AND (PACLITAXEL OR TAXOL)/TI,CN,CT  
 L89 15 S L88 NOT DEOXYCYTIDINE

FILE 'CANCERLIT' ENTERED AT 12:21:06 ON 15 DEC 2002

L90 1610 S L68  
 L91 8604 S L71  
 L92 3 S L90 AND L91

FILE 'EMBASE' ENTERED AT 12:21:40 ON 15 DEC 2002

L93 17936 S L68  
 L94 12253 S L71  
 L95 78 S L93 AND L94  
 L96 50 S L95 AND PY<=1999  
 L97 43 S L96/ENG  
 L98 18 S L97 NOT AB/FA  
 L99 25 S L97 NOT L98

FILE 'BIOSIS' ENTERED AT 12:24:22 ON 15 DEC 2002

L100 8 S L95  
     SEL DN AN 3  
 L101 1 S L100 AND E1-E2  
 L102 3 S L100 AND (AU ? OR WIENTJES ?)/AU  
 L103 3 S L101,L102

FILE 'BIOSIS' ENTERED AT 12:25:55 ON 15 DEC 2002

FILE 'WPIX' ENTERED AT 12:26:13 ON 15 DEC 2002

L104 807 S L19 OR L20  
     E STAUVIDINE/DCN  
     E SANILVUDINE/DCN  
     E D4T/DCN

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      E D-4T/DCN
      E D 4T/DCN
      E AZT/DCN
      E E3+ALL
L105      389 S E2
L106      7 S DIDEOXY(L)DIDEHYDROTHYMIDINE
L107      937 S L104-L106
L108      59 S STAVUDIN?
      E STAVUDIN/DCN
L109      937 S L107,L108
L110      1353 S L23
      E TAXOL/DCN
      E E3+ALL
L111      763 S E2
L112      1468 S L110,L111
L113      23 S L109 AND L112
L114      1 S L113 AND (AU ? OR WIENTJES ?)/AU
      E R11606+ALL/DCN
L115      90 S E1
L116      23 S L115,L109 AND L112
L117      1 S L114 AND L116
L118      22 S L113,L116 NOT L117
L119      12 S (P631 OR P632 OR P633 OR P630)/M0,M1,M2,M3,M4,M5,M6 AND L118
L120      8 S (B14-H01 OR C14-H01 OR B14-H01A OR C14-H01A OR B14-H01B OR C1
L121      0 S (B14-S09 OR C14-S09 OR B12-C09 OR C12-C09)/MC AND L118
L122      12 S L119,L120
      SEL DN AN 7 9 L122
L123      2 S E1-E4
L124      3 S L117,L123 AND L104-L123
L125      10 S L118 NOT L122

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FILE 'WPIX' ENTERED AT 12:38:04 ON 15 DEC 2002